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Review article

ETHICAL AND LEGAL ASPECTS OF FUNCTIONING OF ETHIC COMMITTEES IN BULGARIA

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SUMMARY:

Scientific research has to be based on ethical standards that promote the protection of human rights.

On a national level, the domestic legislation of the Republic of Bulgaria foresees a procedure for obtaining an opinion from the Ethics Committee for Multicentre Trials in order to introduce a substantial change in a clinical trial and non-interventional study. The procedure aims to evaluate the compliance of the planned clinical trial with the norms of good clinical practice, the requirements of the Medicinal Products in Human Medicine Act. On European Union level, standards have been set down in Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use.

The licensing regime that has been introduced on a national level requires the performance of documentation evaluation that addresses a major change in a clinical trial and non-interventional research. Legal definitions of the terms "principal investigator" and "coordinating investigator" have been introduced. The "principal investigator" is the medical doctor or the dentist, designated by the sponsor, who leads the overall execution of the clinical trial in accordance with the approved protocol and good clinical practice guidelines and is responsible for the researchers. The "coordinating researcher" is a researcher appointed to coordinate researchers from different centres participating in a multicentre trial.

Ethic committees performing review have to provide independent advice on the extent to which a biomedical research proposal complies with recognized ethical standards. Scientific research must necessarily conform to commonly accepted scientific principles and be based on thorough knowledge of scientific literature and other relevant sources of information.

Keywords: Ethic committees, legislation, competences, standards

Healthcare is a complex system that includes activities of management, financing and provision of health services aimed at improving the health status of the country's population. The modern health system is based on the principles of solidarity, choice of efficiency in spending resources on the system and, by its very nature, has both social and economic characteristics. The health care sector is unusual in the extent to which private providers are entrusted with important public roles, and the large amount of public money allocated to health spending in many countries. [1]

The role of the State in healthcare systems in most countries is still paramount, although the world's tendencies are towards increasing the liberalization in healthcare services market and the developing competitive environment. Various topics related to medicine have been challenging nowadays including high costs of treatment, associated pressures to cut costs, lack of availability of health insurance, etc. [2]

Healthcare encompasses systems designed to offer healthcare services to patients – no matter if regards to prophylaxis, to diagnosis, to treatment or to palliative care - with the ultimate goal of improving one's health. Healthcare systems have a central role in modern society, by providing people with the opportunity to take care of their own health and to improve it. Due to the proper functioning of healthcare systems and the provision of high quality healthcare services, we are able to live better and more intensive live.

Ethics committees developing activities in facilities providing healthcare services are functioning based on the principles of medical ethics and medical law. Such committees have several main functions including draft conclusions on patients' complaints regarding healthcare services, as well as carrying out investigations on unethical relationships between hospital personnel and patients or between patients and trainee students and postgraduate students when professional services are provided at healthcare facilities.

Sometimes ethic committees' competences involve monitoring activities on compliance with the legal requirements for clinical trials of medicinal products, medical equipment and medical devices.

Scientific research has to be based on ethical standards that promote the protection of human rights. [3] Scientific research must necessarily conform to commonly accepted scientific principles and be based on thorough knowledge of scientific references and other relevant sources of information. Individually identifiable health information should be collected, used, and/or disclosed only to the extent necessary to accomplish a specified purpose(s) and never to discriminate inappropriately. [4]

The current legal, regulatory framework in regard to the essence, functions and competences of ethic committees is complex and multi-layered, including regulation on both constitutional and legislative level, as well as a number of legal acts transposing the relevant Directives adopted within the European union. Various guidelines concerning conducting clinical trials are also introduced in national legal acts.

On a national level, the domestic legislation of the Republic of Bulgaria foresees a procedure for obtaining an opinion from the Ethics Committee for multicentre trials in order to introduce a substantial change in a clinical trial and non-interventional studies. This procedure has been implemented pursuant to article 130, para. 1 in conjunction with article 103, para.1 and article 109, para.1 of the Medicinal Products in Human Medicine Act. The procedure aims to evaluate the compliance of planned clinical trial with the norms of good clinical practice, as well as with the requirements of the Medicinal Products in Human Medicine Act and Regulation (EC) No. 1901/2006 of the EuropeanParliament and of the Council of 12 December 2006 on medicinal products for paediatric use.

Bulgarian national legal acts regulating the functioning, structure and activities of ethical committees established on national bases have been introductingon both statutory and secondary legislation.

Main legislative acts include:

– Health Law – in force of January 1st, 2005

– Medicinal Products in Human Medicine Act - in force of April 13th, 2007

– Law on Medical Devices – in force of July 12th, 2007

– Law on professional associations of doctors and doctors of dentistry - in force of January 1st, 2007

– Ordinance No. 31 of August 12th, 2007 establishing rules for good clinical practice

– Ordinance on the essential requirements and procedures for assessment of the compliance with the essential requirements of medical devices under the article. 2, para. 1, item 3 of the Law on Medical Devices. – published in State Gazette, issue 65 of August 10th, 2007

– Ordinance No. 2 of February 5th, 2008 on the requirements for collection, validation and provision of information on unwanted side effects and on the content and format of emergency reports for adverse drug reactions and periodic safety reports

– Ordinance No. 27 of June 15th, 2007 on the data requirements and the documentation for the authorization and the registration of medicinal products - published in State Gazette, issue 54 of July 3rd, 2007

– Ordinance No. 15 of April 17th, 2009 on the conditions for issuing a manufacturing or import authorization and the principles and requirements of good manufacturing practice for all types of medicinal products, clinical trial medicinal products and active substances - published in State Gazette, issue 38 of May 22nd, 2009

– Ordinance No. 18 of June 20th, 2005 on the criteria, indicators and methodology for accreditation of healthcare facilities.

– Code of professional ethics of doctors in Bulgaria, published in State Gazette issue 79 of Sept. 29th, 2000

– Rules and Regulations of the Central Ethics Commission to the Council of Ministers on the Law of Medicinal Products in Human Medicine - published in State Gazette issue 81 of Oct. 9th, 2007

– Rules for procedure of the commission for professional ethics of Bulgarian Medical Association, adopted by the professional ethic committee at the Bulgarian Medical Association on June 19th, 2015

According to article 29, para. 2 of the Constitution of the Republic of Bulgaria, "no one shall be subject to medical, scientific or other interventions without his or her voluntary written consent". [5] According to article 17, para 4 of the Law on medical facilities, clinical trials are conducted in regard to the Law on Medical Products in Human Medicine. [6] This legal act requires that the conduction of clinical trials has to be based on ethical principles and in accordance with the fundamental principles of the protection of human dignity as established under the Helsinki Declaration. Clinical trials need to be conducted in accordance with the principles of Good Clinical Practice as required by Regulation (EC) 1901/2006. [7]

There are numerous codes of ethics establishing rules and principles in relation to clinical trials such as the Professional Ethics Code, the Ethics Code of the Bulgarian Association for Clinical Trials and the Ethical Codes of the Research Pharmaceutical Industry and Generic Pharmaceutical Manufacturers.

The legislative framework of clinical trials in Bulgaria adopts and introduces European and international rules and standards in regard to planning and conducting clinical trials. Legal definitions of the terms "principal investigator" and "coordinating investigator" have been introduced.

A major change in the performance of clinical trials and non-interventional researches has been achieved as introducing the performance of documentation evaluation.

The "principal investigator" is the medical doctor or the dentist, ho leads the overall execution of the clini-

cal trial in accordance with the approved protocol and good clinical practice guidelines. The "coordinating researcher" is a researcher appointed to coordinate researchers from different centres involved in a multicentre trial.

The Law on Medicinal Products in Human Medicine regulates public relations relating the authorization and supervision of the manufacture, use, clinical testing, advertising, import, trade, classification, pharmacovigilance and pricing of medicinal products for human use, as well as the preparation on Positive Drug List. The aim of the law is to create conditions that ensure the placing on the market of medicinal products that meet quality, safety and efficacy requirements. Through this legislative act the harmonization of the Bulgarian drug legislation in accordance with the EU drug legal framework has been achieved and at the same time conditions have been created to guarantee the use of medicinal products that meet the requirements for quality, safety and efficacy.

This law explicitly states that clinical trials may be conducted in compliance with the fundamental principles of human rights and human dignity in regard to protection of any medical and biological study under the Helsinki Declaration and only in hospital care facilities, mental health care centres, Health care centres of skin-venereal diseases, complex oncology centres and diagnostic-consultative centres, which have received a positive accreditation assessment for overall activity. Accreditation has also been required for activities performed in a functional medical institution conducting a clinical trial, in accordance with the Law on the medical institutions.

Particular attention has been paid to clinical trials on minors and adults unable to express their consent freely. The rules on informed consent and the right of withdrawal such consent during the clinical trial performance are being regulated in details. According to the law, liability in case of injuries or deaths caused by or in connection with the conduct of the clinical trial is allocated between the sponsor and the principal investigator.

Tests involving humans are divided into 4 phases:

The Clinical Trial in Phase 1 is the first application on patients of the biologically active substance. It is usually performed with the participation of 10 to 20 healthy volunteers in hospitals that have the necessary equipment to conduct such trials. The study aims to determine the pharmacokinetics (i.e., absorption, distribution, metabolism and excretion) of the tested compound, as well as its tolerability.

The Clinical Trial in Phase 2 is the first application of the biologically active compound in patients. It aims to determine its effectiveness, optimal dose and preliminary safety data. Potential differences in pharmacokinetic behavior between healthy volunteers and patients are sought. Several hundred patients are involved in this phase.

The Clinical Trial in Phase 3 aims to investigate the therapeutic relevance, i.e., safety and comparative performance of the product. At this stage, a large number (up to several thousand) patients are involved. Normally, regulatory authorities require the trial to be conducted in a comparative and randomized manner.

The Clinical Trial in Phase 4 is performed after Marketing Authorization (post-marketing stage) has been obtained. In this phase, unlike in phases 2 and 3, the long-term use of the product is being studied, following the adverse events that may accompany its use. During the 4th phase, new indications and dosing regimens of the drug are studied, as well as mechanisms of action of the product.

Ethical committees functioning in medical institutions are designed to help doctors and other medical and non-medical specialists, patients and their families inregard to ethical and legal dilemmas they are facing in everyday practice. Committees on professional ethics provide support and professional, competent opinion to healthcare professionals in regard to their responsibilities in medical practice and professional organizational activities. One of the most significant contributions of ethic committees is related to their participation in the regular updating of professional ethic codes. They analyse, explore, compare and systematize the moral norms and values of the healthcare profession. At the core of professional ethics is the category of professionalism, liability and responsibility.

The competences of the Ethics Committees established in the medical institutions in Bulgaria, is related to regulation of the structure and activities of healthcare facilities, as it is possible for the director of the institution to establish a separate code of conduct in regard to ethical attitude in providing healthcare services.

Regulated rules ensuring high standards of ethical conduct are respected by all persons involved in the medical-diagnostic process and overall medical practice, as well as researchers and research team members at every stage of research conducted within the medical institutions.

The current legislative framework allows only a certain range of medical and biological researches to be regulated, which requires synchronizing the activities performed currently by the existing ethics committees within medical institutions in Bulgaria, as this could help in elaboration of a model for optimizing their activities.

Legal, regulatory framework regarding ethic committees competences has not been detailed, as contradictory practices have been observed, due to the fact that a model for optimization of their activities has not been introduced. Appropriate actions toward synchronizing the activities of the ethics committees Bulgaria could have positive effect on the healthcare system in Bulgaria. Regulatory measures could lead to the improvement of the quality of assessment of the ethical norms of conduct in healthcare institutions, as it provides bases for upgrading the quality of the performed healthcare activities.

REFERENCES:

1. Deliversky J. How does corruption affects healthcare sector in Bulgaria. *J of IMAB*. 2016 Jan-Mar; 22(1):1088-1090. [CrossRef]

2. Vodenicharova A, Popova K, Yanakieva A. Leading the change in medical practice: the role of bioethics, *International Journal of Research in Management & Social Science*. 2015 Jan-Mar;3(1):60-63

3. Vodenicharova A, Zlatanova-Velikova R, Yanakieva A. The need of ethical norms within the healthcare management activity. *Health Policy and Management.* 2017;17(1):49-50.

4. Deliversky J. Health Information technology in exchange of health information. *J of IMAB*. 2016 Apr-Jun;22(2):1182-1185. [CrossRef]

5. Constitution of the Republic of Bulgaria, State Gazette No. 56/ 13.07.1991

6. Medical Products in Human Medicine Act, State Gazette No. 31/ 13.04.2007

7. Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/ 92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004. [Internet]

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