

# ETHICAL REVIEW OF BIOMEDICAL RESEARCH IN BELARUS: CURRENT STATUS, PROBLEMS AND PERSPECTIVES

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## **Abstract**

*The paper provides description of the system of ethical review for biomedical research in Belarus, with special emphasis on its historical background, legal and regulatory framework, structure and functioning. It concludes that the situation with research ethics in Belarus corresponds to the tendency of bureaucratic approach to establishment of systems of ethical review for biomedical research, observed in a number of countries of Central and Eastern Europe. Different social, economical and political factors of transition have major impact on capacities of the Belarusian RECs to ensure adequate protection of human subjects. Among the main problems identified are non-equivalent stringency of ethical review for different types of biomedical research; lack of independence, multidisciplinary, pluralism and lay representation experienced by RECs; low level of research ethics education and transparency of RECs activities. Recommendations are made to raise the issue of research ethics on the national agenda in order to develop and maintain the research ethics system capable to effectively protect research participants and promote ethical conduct in research.*

**Keywords:** *research ethics, research ethics committees, Belarus.*

## **Introduction**

During the last decade, a growing interest to the issues of development and operation of the systems of ethical review for biomedical research in Central and Eastern Europe (CEE) has become a visible trend in bioethics literature worldwide [1,2,3]. Attributable to such interest are serious concerns with regard to capacities of CEE countries to

maintain high scientific quality of research and ensure adequate protection of human subjects involved. Indeed, these concerns seem to be quite justifiable, taking into account that increasing volume of health research, witnessed across the region, takes place in a quite specific environment of social, economical and political factors of transition [4].

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Although the overall number of publications on the topic is not very high, it seems that some parts of the region have received more attention and analysis than others. One can see that the overwhelming majority of publications are devoted to either countries recently become European Union (EU) new member states or those planning to do so (candidate countries). To date, little is known about the current status of research ethics in Eastern European countries, belonging to the Commonwealth of Independent States (CIS). This paper attempts to fill (at least in part, to the extent available data allows) this informational gap by providing an overview of the system of ethical review for biomedical research in Belarus, with special emphasis put on its historical background, legal and regulatory framework, structure and functioning.

The current study is in fact a continuation of a larger comparative study of Ethics Committees in CEE, commenced in 2008 within the framework of Advanced Certificate Program in Research Ethics in CEE\*. Various sources of information were used to collect as much data as possible: legal databases, scientific publications, conferences' proceedings and mass-media reports. There was also an attempt to obtain some data on practical aspects of research ethics committees (RECs) work by approaching them via e-mail and offering to fill in a questionnaire, but this attempt proved to be not very successful. Response rate was quite low (out of 52 RECs contacted, only 12 have responded) and therefore not allowing to make valid generalizations. However, this study, with all its limitations, constitutes the first attempt ever to provide comprehensive description of the system of ethical review in Belarus, raise

awareness on its distinguishing features and draw attention to the major problems and challenges.

### **Historical background**

In Belarus, the development of ethical review as a systematic process began in the late 1990s, when the legislative and regulatory framework for biomedical research was introduced in 1999. In contrast to the majority of European countries and the US, where basic elements of ethical review has been developing in a "grass-root" fashion [5,6], in Belarus the system of ethical review has been implemented through a quite rigor "top-down" approach. It was a purely administrative decision of the state authorities, willing to introduce internationally accepted principles of Good Clinical Practice (GCP) into national health research enterprise and open up the local market for multi-centre clinical trials.

However, for that time it was a tremendous progress in the development of research ethics in Belarus, given that prior to that move there were no officially documented activities of ethical review taken place in Belarus. Thus, due to that decision, legislative and regulatory framework for the development and functioning of RECs has been set up. Belarus has chosen an institutional model of ethics review, meaning that ethical evaluation and oversight of research projects are supposed to be performed on a local level. Starting from zero in 1999, the number of RECs had been growing rapidly and by the end of 2000s has reached the number of more than 50 [7]. Since then, the number of RECs has remained at the same level. All RECs are currently located in hospitals, health research institutions and polyclinics (in Belarus, a kind of primary care units).

However, until the mid 2000s, there were no attempts to introduce some degree of centralization and coordination into the RECs system. The problem was addressed by the Ministry of Health (MOH) in 2006, when the National Bioethics Committee (NBC) was established and charged with the task, inter alia, to coordinate and oversight the activity of local RECs [8]. The NBC was also supposed to serve as an appeal body regarding RECs decisions and as a consultative organ providing advice and informational support to local RECs and other governmental and non-governmental organizations on wide spectrum of bioethical issues.

The next important move in the development of ethical review in Belarus took place in the late 2000s, when some amendments to the regulation of clinical trials were introduced. Those amendments aimed at strengthening the role of competent authorities (COA) in the governance of clinical trials, shortening the time limits for ethical review process, as well as changing REC composition by introducing new requirements to REC membership and structure. In fact, those amendments and their implications merit serious attention, since at least some of them deviate significantly from relevant international standards and therefore give rise to justifiable concerns regarding abilities of recently re-shaped RECs to perform their main mission – to protect the rights and interests of research participants from possible abuses of research.

### **Legislative framework**

The basic norms of ethical conduct of biomedical research are embedded in the Constitution of the Republic of Belarus, which states that *“no one shall be subjected without his\her consent to medical or scientific experimentation”*.

Other provisions of the Constitution guarantee safeguarding of human dignity, protection of life, as well as physical and psychological integrity, thus emphasizing the fundamental human values, which constitutes the underlying concept of all regulations governing human research. However, in order to be more than just declarations, constitutional provisions need to be implemented into practice by enactment of relevant legislation, carefully considering social, cultural, economical and political aspects of society in question. No surprise that countries differ in ways and scope of application of universal ethical norms into practice.

In case of Belarus, a remarkable asymmetry in the incorporation of those norms into the legislation and regulation of health research could be detected. In fact, the national legislative and regulatory framework covers only narrow part of the full scope of biomedical research – namely, only clinical trials of drugs and medical devices (CDTs). At the moment, all other types of health research, including clinical trials other than CDTs, research on biological material, epidemiological and psychological studies, fall short of the scope of Belarusian legal acts and regulatory documents.

There are two laws in Belarusian legislation which contain provisions pertaining to legal regulation of clinical trials of drugs and medical devices: the law “On Health Care System” (1993) and the law “On Drugs” (2006).

The law “On Health Care System” introduces basic conditions of legal permissibility of conducting CDTs in Belarus. According to the Law, research on humans is only allowed if the safety of investigational products have been proved beforehand in pre-clinical trials. The Law prohibits research on prisoners,

military personnel, orphans and the legally incapacitated, as well as on mentally ill persons hospitalized under court order. Research on pregnant women and minors is only permitted if the particular trial is intended to test a drug or device relevant to health care for those specific groups of patients. For research on minors, obtaining a proxy consent is required.

The law “On Drugs” introduces the definition and terms of reference for “ethics committee”: according to the Law, “ethics committee is an expert body established within a health care organization, whose responsibilities are to ensure the protection of the rights, safety and well-being of trial participants, provide decision on ethical acceptability of the proposed research, and assess the scientific qualification of researchers and suitability of facilities with regard to particular trial”. However, the Law contains only general characteristics of REC as such and does not provide any details on its establishment, membership, structure and operations.

### **Regulatory framework**

In Belarus, ethical review of clinical trials is regarded as an integral element of a larger system of state control over processes of registration and safety oversight of drugs and medical devices. The Ministry of Health (MOH) is the main regulator of the system. A set of relevant regulations, accompanied with establishment of competent bodies, has been introduced by the MOH with the aim to implement a regulatory and institutional framework for governance of clinical trials.

With regard to ethical review it is stated in all relevant documents that no trial should be commenced without prior REC approval and final authorization given by the MOH. In Belarus, clinical

trials of drugs and medical devices are carried out only in state health care organizations and research institutions, accredited by the MOH through official procedure. Among numerous requirements for receiving such an accreditation, the establishment of a REC within respective organization (institution) is a necessary condition. However, accreditation of a REC itself is not required. It is assumed that in every particular case, the hospital authorities guarantee that the REC structure and operations are in compliance with relevant criteria on membership, composition and standard operating procedures described in specific regulations.

It is an obligation of the sponsor to seek a trial site best suited to the needs of a particular trial. However, the choice is limited by the scope of the register of accredited organizations (institutions), hosting local RECs. In Belarus, the procedure of so called “single opinion” for multi-centre clinical trials has not been introduced into practice yet, involvement of all local RECs in protocol review in case of multi-clinical research is therefore required. A favorable opinion by the REC is not a sufficient condition for trial commencement, a set of relevant documents (registration dossier) should pass expert evaluation at a specific body – the Centre for Expertise and Testing in Health Care (CETHC).

Despite the fact that Belarusian RECs are operating within a strongly centralized and strictly regulated system of a state control over clinical trials, it seems that the RECs system itself is not as centralized and well regulated as the whole system is. Although there were some attempts to introduce some degree of control and coordination over RECs activities by charging the NBC with this task, until now no elements of control

have been implemented into practice. Currently local RECs are accountable to no one. There are no procedures of audit and monitoring of RECs are in place, as well as there are no requirements for local RECs to report results of their work to relevant bodies and inform the public about the most important activities.

### **Membership and composition of RECs**

In Belarus, the regulation of membership, composition and operations of RECs has been changed over time. According to the “Rules for conducting clinical trials” (1999), a REC had to be composed of at least five members, including at least one member whose primary area of interest should be in a non-scientific area and at least one member who had to be independent of the institution/trial site.

In its turn, the “Guidelines on organization and working procedures of RECs” (2000) further specified the requirements on membership and composition of RECs, stating that a REC had to be composed of no less than five, but no more than twelve members, be age and gender balanced. REC composition had to include at least two members without medical education, and it was stipulated that one of them had to be independent of the institution/trial site. Besides health professionals, RECs had to be composed of scientists, lawyers, and experts in human rights issues. However, those “soft laws” had been in power for only less than a decade, having been recently replaced by the new regulations, namely, the “Technical Code of established clinical practice” (2009) and the “Statement on RECs” (2008).

According to the recently introduced “Technical Code of established clinical practice”, a REC should consist of “a reasonable number of members, who

collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial”.

The “Statement on RECs” has put requirements regarding REC membership and composition much more straightforward: “a REC should be composed of employees of the health care organization that establishes it”. According to the “Statement on RECs”, RECs may invite consultants and experts competent in special areas of knowledge, but only for providing consultations and advice. De-facto, non-institutional members have been excluded from REC membership, though lay representation is recognized as important factor for REC pluralism and multidisciplinary [8].

These documents do not contain formal requirements with regard to initial training as well as ongoing education for RECs members. Apparently, the practical work on the committee is perceived as the main method of acquiring appropriate competence for REC members. It should be noted, however, that the basic knowledge on research ethics among health professionals in Belarus, which could be regarded as foundation for improving certain practical skills, is absolutely insufficient, because of extremely low attention paid to bioethics on undergraduate and postgraduate level of medical education [9].

### **Functions and operations of RECs**

Organizational procedures and functions of Belarusian RECs are based on internationally recognized standards of GCP and formulated in the “Technical Code of established clinical practice”, being assembled in so called standard operational procedures (SOPs). Every local REC must adopt SOPs into its own practice and act in accordance with such procedures, thus ensuring uniformity of

REC operations across the country.

The “Statement on RECs” requires that REC members are to be nominated by the administration of the institution which is responsible for REC establishment. The list of REC members has to be approved by the Head of a health care organization (institution). REC members elect a chairperson and a secretary, whose duties are to run organizational and administrative activities. The frequency of REC meetings is not specified, implying that REC members gather on necessity. The quorum is 2/3 of the members, and final decision has to be reached by the majority vote

The scope of REC review should include assessment of ethical, scientific and methodological aspects of the proposed trial. According to the “Technical Code of established clinical practice”, a REC has to consider a number of criteria, including: scientific qualification and clinical experience of the investigators and staff involved, the suitability of facilities in which the trial shall be conducted, the appropriateness of the protocol to the objectives of the trial, the scientific merit of the proposed project, the risk/benefit relationship, the extent to which the health of the participants of the research is monitored during the trial, the measures implemented with regard to the protection of identity and confidentiality of data, the procedures of obtaining informed consent and involvement of vulnerable subjects, the issues of insurance or indemnification covering the sponsor responsibilities, as well as payments and rewards offered and given to the participants.

According to the “Statement on RECs”, a process of reviewing of a proposed trial by a REC (including issuance of the opinion) should not

exceed 30 days after acceptance of an application.

Not a single REC in Belarus, and the NBC as well, has its own website. In fact, the absence of publicly available databases or registers containing general information on clinical trials performed makes it quite difficult to access the data on RECs’ annual workload and the nature of reviewed projects. Very scarce and incomplete information from returned questionnaires suggests that for RECs that are relatively active, the number of annually reviewed protocols is ranging approximately between 3-4 protocols per year. The only source for relevant data is the CETH website which provides information regarding annual scope of CDTs performed in Belarus for the period of 2006 - 2008: in 2006 there were 28 trials (among them 9 multi-centre), in 2007 - 23 (8 multi-centre), in 2008 - 28 (9 multi-centre) [10]. However, it is unknown how many protocols had been rejected for this particular period and for what reasons.

Both legislation and regulation of CDTs in Belarus are silent about financial aspects of REC review, implying that local RECs are supposed neither to collect fees for review, nor have operational budget, nor have their members to be paid for their work.

### **Discussion**

When it comes to evaluation of effectiveness of any system of ethical review for biomedical research, it should be emphasized that only a narrow focus on regulatory and institutional framework of ethical review will not provide a comprehensive picture of the system as a whole, nor will it detect and explain possible shortcomings and problems in its structure and functioning. Instead, the system of ethical review should be viewed from much broader perspective,

by taking into account a wide spectrum of social, economical, cultural and political factors, all of which have strong influence on current status of ethical review in the respective country [11]. Recognizing this, the most important questions, needed to be answered when considering the effectiveness of any ethical review system, especially in a country in transition, can be formulated as follows: is the system really working? Is it fit for purposes assigned to it? Is it able to perform its functions properly?

In the absence of commonly agreed standards and precise criteria for the assessment of effectiveness of any ethical review system, answering to the aforementioned questions appears to be quite difficult [12]. However, one can notice that when it comes to evaluation of the system of ethical review for biomedical research in a particular country or region, several topics always attract more attention and are more intensively discussed in the bioethics literature than others. For the CEE region, such topics are: scope of research covered by ethical review, independence of RECs, composition, motivation and competence of RECs members, management of conflict of interests, transparency and procedural clarity of ethical review [13,14,15]. The situation in Belarus can be discussed in the light of these problematic areas, which are quite illustrative for indicating the level of progress a particular country has achieved in developing its own system of ethical review for biomedical research.

As it has been already mentioned, CDTs are granted somehow “privileged” position amongst the wide spectrum of different types of biomedical research in Belarus. Such an imbalance of regulations with regard to ethical review of different types of biomedical research can at least partly be explained by

referring to the historical background and actual motives laid behind the establishment of the system of ethical review in Belarus. It seems that in Belarus the process of development of the system of ethical review has been strongly influenced by pharmaceutical companies and has been aimed mostly at meeting formal requirements needed for inclusion of local market in the international enterprise of multi-centre clinical trials. In this regard the situation in Belarus corresponds to the tendency of bureaucratic approach to establishment of a system of ethical review, which has been observed in some other CEE countries [16]. It has been stated that this tendency stems from common Soviet legacy of authoritarian style of regulation, covering every aspect of social life, including health care. Belarus has inherited much from the Soviet times, so the domestic variation of non-equivalent stringency of ethical review, resulting in extremely inadequate level of protection of human subjects, who are participating in different types of biomedical research, can at least partly be explained by preservation of traditional dominance of interests of the state over individual rights of its citizens.

It seems that Belarusian health authorities do not give great value to multidisciplinary and pluralism of RECs, as non-institutional members have been recently excluded from REC membership and lay representation has been deliberately reduced to a minimum. In the absence of any official statements explaining rationale of changing the regulation of ethical review, it could be assumed that by this move the health authorities have addressed the problem of the system’s inability to attract potential candidates with appropriate qualification for REC membership from outside of hosting institutions. Nevertheless, instead

of introducing some incentives and motivators for REC members, the national health authorities have come to the decision of truly bureaucratic character, perfectly corresponding to the logic of the traditional command style of governance. Although it is difficult at the moment to estimate correctly the effect those changes could render on quality of ethical review and adequacy of research subjects protection, it is apparent that this move constitutes a significant step back in the development of research ethics in Belarus.

It could be concluded that the limited transparency of ethical review in Belarus leads REC members to formal and bureaucratic approach to fulfilling their tasks. In the absence of reliable and easily accessible sources of information on research ethics, both REC members and researchers may share some sorts of misconceptions about the nature, scope and purpose of ethical review. As Vents Silis points out, “...at the foundation of ... misconceptions is the lack of information about contemporary research ethics, which is a well-reasoned and methodical assessment of the ethical aspects of scientific research, designed to foster responsible conduct, thereby being an integral part of good scientific practice in general, and especially of research involving humans” [15]. Therefore, such misconceptions could be addressed quite effectively by rising awareness on research ethics issues among professionals and the public, and ensuring transparency of ethics review through increasing availability of data concerning RECs’ activities.

Another problematic area revealed by the study pertains to the insufficient level of bioethics education and lack of motivators provided for REC members in Belarus. In fact, for REC members, the only way to acquire some knowledge and

skills on research ethics is through self-education and practical work on the committee. Furthermore, REC members are not given any compensation for the costs associated with ethical review, as well as they are not offered any non-monetary incentives, such as career promotion or opportunities to attend conferences and workshops. As Vilius Dranseika and colleagues conclude regarding the situation in the Baltic States: “In general, the lack of motivators can both result in poorer quality of ethical review and reduction in the number of interested potential candidates” [14]. It seems that this statement could be applied to the situation in Belarus as well, which means that the current approach to the organization and functioning of the system of ethical review in Belarus can be characterized as a “vicious circle”, which is only able to exacerbate problems instead of solving them. At the same time, in the situation when complexity and volume of biomedical research is constantly increasing, comprehensive assessment of methodological, scientific and ethical aspects of proposed studies is becoming quite difficult task for RECs. This task can be fulfilled by only competent and purposeful REC members who have been adequately trained and motivated. As Christiane Druml and colleagues state: “The future of ethics committees can only be the small but professionalized committee of highly qualified and trained experts who are adequately paid for their contribution as an integral part of clinical research” [17].

### **Concluding remarks**

In a relatively short period of time, a legal, regulatory and institutional framework for ethical review of biomedical research has been developed

in Belarus. As the actual study shows, the national system of research ethics review basically adheres to international standards. However, significant shortcomings in the system's structure and functioning have been revealed. No surprise that those quandaries are similar to problems faced by other transitional countries of the CEE region. However, one can notice the difference in approaches these countries use to overcome the difficulties and ensure adequate level of protection for research participants. In Belarus, the system of research ethics review has been established and regulated in a quite rigid and bureaucratic manner, evidently failing to promote such vital characteristics of ethics review as its equivalent stringency for different types of biomedical research; independence of RECs; multidisciplinary, pluralism and lay representation in their membership and structure; sufficient level of research ethics education and transparency of RECs activities. With these features being apparently underdeveloped, there is a threat for Belarusian RECs to become rather formal structures, serving just for, as Richard Ashcroft points out, "*more to satisfy foreign partners' or research sponsors' requirement, rather than to address problem or concern to patients*" [18].

Given that such a rigid and bureaucratic approach to establishment and regulation of the system of ethics review stems from deeper historical background of contemporary Belarusian society and therefore should be viewed from broader socioeconomic, cultural and political perspective, it can be

assumed that only separate efforts focused on capacity building of local RECs would probably be ineffective. Rather, there is a need for "*moving from research ethics review to research ethics system*", which, according to Adnan Ali Hyder and colleagues, means concerted efforts from the side of not only health authorities, but researchers, institutions and national governments as well [11]. It also means that problems of research ethics should not be regarded as issues related to only narrow sphere of pure science, but should be raised on the national agenda in order to establish and maintain the research ethics system able to effectively protect research participants and promote ethical conduct in research. Hopefully, the current analysis of the system of ethics review in Belarus would contribute to such a movement.

\* The project was supported by Research Grant # R25TW007085 from the National Institutes of Health - Fogarty International Center (USA). The content is solely the responsibility of the author and does not necessarily represent the official views of the Fogarty International Center or the NIH.

### **Acknowledgement**

I am very grateful to my teachers from the Advanced Certificate Program in Research Ethics in CEE Countries – Martin Strosberg, Eugenijus Gefenas, Andres Soosaar and Vents Silis, for their continuing support, encouragement and helpful suggestions on the structure and content of the paper.

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