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Research ethics in the context of transition: gaps in policies and programs on the protection of research participants in the selected countries of Central and Eastern Europe

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Abstract

This paper examines the ability of countries in Central and Eastern Europe (CEE) to ensure appropriate protection of research participants in the field of increasingly globalizing biomedical research. By applying an analytical framework for identifying gaps in policies and programs for human subjects protection to four countries of CEE – Belarus, Latvia, Lithuania, and Poland, substantial gaps in the scope and content of relevant policies and major impediments to program performance have been revealed. In these countries, public policies on the protection of research participants lack consistency and reliable mechanisms for their implementation. Impediments to program performance most often relate to inadequacies in the national research ethics systems with regard to organizational structure, budgetary support, supervision, and training. The level of research ethics capacity varies from country to country and depends on socio-economic and political factors of post-communist transition. The breadth and depth of the problems identified suggest that the current level of protection for research participants in CEE might be inadequate to the challenges posed by the globalization of biomedical research. In CEE countries, there is a need for strengthening research ethics capacity through modification of relevant policies and improvement of program management. The differences among the countries call for further research on identifying the best approaches for filling the gaps in the policies and programs aimed at ensuring effective protection of research participants.

Keywords

research ethics; public policy; Central and Eastern Europe

Introduction

In the past decade, the region of Central and Eastern Europe (CEE) has experienced explosive growth in biomedical research with human participants. Across the region, the amount of registered health research has more than tripled over the past decade (Gambrill 2008). According to the European Medicines Agency, the number of patients involved in clinical drug trials conducted in the countries of the former Soviet Union increased from 664

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in 2005 to 10.737 in 2011, and the number of investigator sites increased from 72 to 807 for the same period (EMA 2013). The ClinicalTrials.gov database, which contains all public and privately funded clinical trials subject to the U.S. Food and Drug Administration, lists over 15.000 trials which are located in the CEE region (U.S. Department of Health and Human Services 2015). A large proportion of the research involves multi-centre clinical trials of new drugs and medical devices, which have been driven by transnational pharmaceutical corporations and sponsored from abroad (Caldron et al. 2012). The region is increasingly considered an attractive place for conducting biomedical research because of the availability of a relatively well developed healthcare infrastructure and an extensive population of potential research subjects – factors which allow transnational companies to conduct high quality research at lower costs and at a much faster pace than in Western countries (Clark 2009, p. 8; Drakulich 2009). However, concerns have been raised that the rate at which biomedical research in the region is being expanded is outpacing the ability of CEE countries to establish and maintain strong and reliable research ethics systems (Global Forum on Bioethics in Research 2007). The danger is that outside sponsors might take advantage of this weakness and choose a research site out of an expectation of a less stringent regulatory regime and likely approval of studies which would be rejected elsewhere. The concerns over the research ethics capacity of CEE countries are further exacerbated by the scarcity of the information on the structure, functions, and performance of the relevant systems. The specific socio-economic and political environment in the region is also an issue: the countries of CEE are still moving from authoritarianism to democracy and their basic social institutions, including health systems and biomedical research enterprises, are undergoing significant changes (Rechel and McKee 2009).

The goal of this paper is twofold: (1) to address the concerns raised over the ability of CEE countries to ensure adequate protection of human research subjects and (2) to identify gaps in policies and programs for human subjects protection in the selected countries of CEE, and analyze them from public policy perspective. To reach the goal, available information on research ethics policies and programs in the selected countries of CEE has been analyzed in a systematic and comprehensive way. The *Background* section provides a short description of research ethics systems in the selected countries of CEE, with special emphasis given to historical aspects of their development and most prominent features of their legal and regulatory framework. The *Methodology* section describes the framework used for identification of gaps in policies and programs on research ethics in the selected countries of CEE. The main part of the paper is concerned with the issue of how plausible the national research ethics policies and programs in these countries are in terms of their ability to achieve officially proclaimed goals of ensuring the protection of human subjects. Furthermore, there is an exploration of how and to what extent the factors of post-communist transition affect the development and implementation of research ethics policies and programs. In the final part of the paper, the needs of CEE countries regarding improvement of their research ethics systems are identified. The *Conclusion* section reflects on directions for further research and encourages the use of the study results for strengthening the research ethics capacity of CEE countries.

Background

The development of ethical review of biomedical research in CEE countries as a systematic process began in the early 1990s, when the Soviet Union and the Eastern Bloc collapsed (Glasa 2000). After obtaining independence, newly sovereign states had a chance to build their research ethics systems "from scratch" by adopting existing models of research ethics review from Western countries. Further development of research ethics in CEE resulted in the establishment of national systems for human subjects' protection, which differed considerably in terms of structure, functions and performance. The majority of countries in CEE have adopted an institutional model of ethical review, where review of research projects takes place in the same institution where the research is carried out (Glasa 2000). However, some countries (e.g., Latvia and Lithuania) have adopted a regional model, where review is conducted on a regional level (Dranseika et al. 2011).

Just knowing what kind of a model of ethical review is in place in a particular country provides little guidance in deciding whether or not the country is doing well in terms of protection of research participants. In the bioethics literature there is a diversity of opinion with regard to the pros and cons of institutional and regional models, but there is nevertheless consensus that it is not the model of ethical review that determines the effectiveness of the system for human subjects protection (Edgar and Rothman 2003; Emanuel et al. 2004; McNeil 2007). Far more important are the functional aspects of the system, which characterize its ability to accomplish assigned tasks. In order to assess research ethics systems in terms of their functionality, a broader view needs to be taken on the complex set of interactions between their internal elements and external factors of social and political environment.

Methodology

This is a descriptive study which is part of a larger comparative study of ethics committees in CEE commenced in 2008 within the framework of the Advanced Certificate Program in Research Ethics for CEE[1]. To date, systematic descriptions of research ethics systems have been provided for Baltic countries (Dranseika et al. 2011; Silis 2010) and Belarus (Famenka 2011), thus making it possible to compare research ethics systems belonging to countries with different socio-economic and political environments. Also, valuable information has recently been provided on the system of regulation and oversight of clinical trials in Poland (Waligora 2013) - the country which hosts the highest number of clinical research trials in the region (EMA 2013). For purposes of this study, an analytical framework for identifying gaps in policies and programs for human subjects protection, which has been developed by the co-directors of the Advanced Certificate Program, Martin Strosberg and Eugenijus Gefenas (Strosberg et al. 2014), has been applied to research ethics policies and programs of the selected CEE countries.

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In this framework, research ethics review is conceptualized as a “program” serving as a vehicle for accomplishing the public policy goal of the protection of human research subjects (Fig. 1). Here, the research ethics review occupies a central position in the research ethics system, similar to the models developed by Adnan Ali Hyder and colleagues (Hyder et al. 2009) and Eugenia Lamas and colleagues (Lamas et al. 2010). The framework delineates research ethics committees (RECs) functioning in terms of the logical flow of structure, process, outputs, and outcomes. Public policy is seen as a flow of inputs in the form of laws, regulations, budgetary support, training programs. Inherent in this conceptualization is the idea that these inputs need to be “managed” toward the policy end. How well program management is carried out is the main point in evaluation of the policy and program performance. The model focuses on program management at two levels: the institutional, regional, or national organizations that directly operate RECs and national level organizations (e.g., national bioethics commission, agencies of the ministry of health) that oversee and support the entire system. The value of the model is that it allows identification of gaps between the policy’s intended goals and what actually happens in reality. Impediments to program management and by extension to program performance may include a lack of necessary policy inputs and a failure to implement key elements of the program structure (Strosberg et al. 2014).

In this study, the main sources of information have been publically available documents (national laws, regulations and guidelines; policies and procedures of individual RECs; reports, audits and materials from official websites), as well as findings of previous studies on national research ethics systems in CEE countries. Examples coming from four countries of CEE - Latvia, Lithuania, Belarus and Poland, have been used in order to analyze the differences these countries have in terms of the protection of human research subjects.

Policies for the protection of human research subjects in CEE countries

In CEE countries, official public policies pertaining to biomedical research declare their ultimate goals as ensuring the protection of research participants to the maximum extent possible, while advancing research, science and technology in order to improve health of the population. For the most part, governmental policies in these countries draw on the internationally accepted standards of research ethics (Silis 2010; Dranseika et al. 2011; Famenka 2011; Waligora 2013). However, a key question here is whether the research ethics policies in CEE really provide a clear, comprehensive and solid foundation for the protection of research participants and whether they are free from gaps which prevent them from being operational and efficient. Strosberg and colleagues compare an official public policy with an architect’s sketch of a building, asking whether the sketch is clear and complete enough to inform the construction and whether any critical piece necessary for the success of the building is missing (Strosberg et al. 2014). When a policy contains only broad statements and aspirational goals (“we are going to construct a perfect building”), without describing ways of how these goals can be achieved in practice, the result can be anything but “Potemkin Village”, and the policy might have only symbolic value and serve for purposes of rhetoric.

Below there are some examples of gaps in official policies pertaining to the protection of human subjects in CEE countries. These examples are drawn from studies which have been conducted by fellows, alumni, and faculty of the Advanced Certificate Program in Research Ethics for CEE. The first example illustrates the lack of policy on ensuring equivalent protection of human subjects participating in different types of research studies.

Non-equivalent stringency of ethical review in CEE

It seems fair to assume that if the ultimate goal of research ethics policy is the protection of research subjects, then the safeguards for participants who are exposed to comparable levels of physical or psychological harm should be ensured equitably. Therefore, the scope of research covered by ethical review in a particular country is an important characteristic of a research ethics policy, as it reflects the extent to which participants of research are protected from possible harm. At the moment, however, official policies in CEE countries require ethical review to be conducted only for research projects that take place within a healthcare context (Gefenas et al. 2010). It means that a wide range of non-biomedical human studies, including sociological, anthropological and psychological research, do not fall within the scope of REC approval, irrespective to the level of risk they might generate. The phenomenon of asymmetry in the power of the regulations pertaining to different types of human research has been described by Gefenas and colleagues in their analysis of the situation in the Baltic countries, and has been defined as "*non-equivalent stringency of ethical review*" (Gefenas et al. 2010). According to the authors, there is the lack of a policy ensuring equivalent protection of human subjects participating in different types of research. However, although it is stated that "the phenomenon… is mostly connected to the patchwork-like nature of different European instruments that regulate different types of research studies" (Gefenas et al. 2010, p. 439), examples from other parts of the region might suggest that the problem lies much deeper than just inconsistencies in the European regulatory documents.

It is important to note that Gefenas and colleagues (2010) have observed countries which are members of the European Union (EU), although many other countries in the region are not members of the EU. In the EU countries, a number of safeguards for participants of biomedical research have been introduced in the process of adjusting and harmonizing of national legislative texts with binding European documents. For example, the legal and regulatory framework for research ethics review in Lithuania has been enforced by a separate piece of legislation - the Law on Ethics of Biomedical Research (2000), which, with its amendments, reflects the influences of different European legal instruments, such as the EU Directive 2001/20/EC on Clinical Trials on Medicinal Products for Human Use, the Council of Europe Convention on Human Rights and Biomedicine and its Additional Protocol on Biomedical Research (Council of Europe 1997; 2005). In the non-EU countries, by contrast, policymakers have been on their own in formulating and introducing policies aiming at ensuring the protection of human research subjects, as there have been no legal obligations imposed on them to follow the practices in the EU. The lack of conditionality, however, has resulted in only fragmentary adoption of the international ethical standards of research into national regulations and led to incompatibility of relevant policies with international documents on research ethics. For example, in Belarus the only type of

research which is legally subjected to ethical review is clinical trials of drugs and medical devices. The wide spectrum of other biomedical and non-biomedical human research is not covered by Belarusian legislation at all. Applying the analogy Strosberg and colleagues (2014) drawn between an official public policy and an architect's sketch to the Belarusian context, it can be concluded that the protection of human subjects in non-clinical research is a major missing piece in the original sketch of a building.

In contrast to the situation in the Baltic States, the situation in Belarus cannot be explained by reference to the inconsistencies in the European regulatory framework alone, as Belarus is neither a member of the EU nor is a member of the Council of Europe. Rather, the Belarusian variation of non-equivalent stringency of ethical review can be regarded as reflection of the preferences national policy makers have towards particular types of human research. It seems that out of the whole set of human research with equal levels of risk, only a few have been taken seriously and attended to in preference to others. What are the reasons for granting such a privileged position to these types of research? Although Belarusian regulations are silent about this, it appears, and perhaps not incidentally, that the preference has been given to the types of research which have a bigger potential for bringing about tangible benefits, such as foreign funds or any other material or intellectual resources.

Management of conflicts of interest in RECs

Another example of gaps in research ethics policies in CEE countries pertains to the management of conflicts of interest among REC members. When observing the research ethics systems of the Baltic countries, Dranseika and colleagues have found that the policies on organization and functions of RECs "rely solely on voluntarily disclosure of potential conflicts of interest" (Dranseika et al. 2011, p.52). However, voluntary disclosure is a widespread mechanism routinely used for the management of conflicts of interest in a number of different countries, provided that the most important principles of REC structure and membership - independence, multidisciplinarity, pluralism and lay representation remain unaffected. Although the criteria for REC composition and membership vary among Baltic countries, they are generally in compliance with the provisions of international guidelines issued by the International Conference on Harmonization (ICH 1996), the World Health Organization (WHO 2000) and the Council for International Organizations of Medical Sciences (CIOMS 2002). Furthermore, the establishment of a regional model of ethical review in Latvia and Lithuania can be regarded as an attempt to enhance REC independence and minimize the possibility of occurrence of conflict of interest among REC members.

In contrast, Belarusian regulatory requirements for composition and membership of REC deviate significantly from international standards. The official policy dealing with regulation of REC structure and functions in Belarus states that "an REC should be composed of employees of the health care organization that establishes it" (Ministry of Health of the Republic of Belarus 2008). The issue of balance between biomedical and non-biomedical representation in REC membership is not further specified in the regulation, making it possible to assume that there could be only a minimum or no lay members in RECs at all. In the situation where non-institutional members are excluded from the ethical review process, and lay representation on RECs has been reduced to a minimum, reliance on only voluntary

disclosure of potential conflicts of interest seems to be rather insufficient protection from possible bias in REC decisions. Here is another example of a missing piece in the imaginary blueprint, as the policy lacking adequate safeguards against conflicts of interest raises questions whether RECs with such a deficient structure and without appropriate protective instruments against undue influence are able to ensure an independent and unbiased review process.

Program management at the local level

According to Strosberg and colleagues, program management is a useful analytical construct for assessing how well the policies are being managed towards an end (Strosberg et al. 2014). At the local level, the program for the protection of human research subjects is managed by organizations that directly operate RECs, and at the national level it is managed by organizations that oversee and support the entire system. Below I explore how the program for the protection of human research subjects in CEE countries is managed at the local level.

The Strosberg and colleagues' framework delineates REC functioning in terms of the logical flow of structure, process, outputs, and outcomes (Fig. 1). As there is no general agreement on objective indicators which can provide a measurement of the quality of the REC work, program assessment typically falls back upon measures of structure and process (Coleman and Bouësseau 2008). Using the analogy of an architect's sketch of a building, it can be said that in order to evaluate the program for the protection of human research subjects one should check if the critical building blocks related to the REC structure and process are in place. In other words, the goal is to find out to what extent the research ethics program is provided with the necessary "inputs" (e.g., authority and political support, budget, training) and key pieces of program structure. In the context of CEE, however, with its notable lack of transparency, getting a clear picture of how inputs actually flow is quite problematic. It is common for researchers in CEE countries to report failures in obtaining direct knowledge from individual RECs and their hosting institutions (Silis 2010; Famenka 2011). In the situation when it is very difficult (or almost impossible) for researchers to directly observe the work of RECs, the main source of information on REC performance is publically available documents.

Budgetary support, transparency and training issues

One of the most sensitive topics associated with REC performance in CEE countries is the issue of budget and payment to REC members. When describing the Latvian research ethics system, Silis (2010) points out that only those RECs which are reviewing clinical trial applications are able to collect fees and pay salaries to the members. With regard to other Latvian RECs, the work of their members is not compensated. In Belarus, regulations on RECs have no provisions on financial issues at all, thus implying that RECs are supposed to neither collect fees for review, nor have operational budget, nor have their members paid for their work. Although the reasons for such budgetary constraints are not stated in the regulatory documents, they might range from deliberate attempts to prevent undue financial inducement for REC members to austerity measures imposed on the health sector as a whole

(Nuffield Council on Bioethics 2002). However, low budgetary priority to research ethics review might also reflect the low level of institutional commitment to the promotion and maintenance of the ethical conduct of research (Hyder et al. 2009). Whatever the underlying reasons might be, the lack of financial support for RECs can have a major negative impact on the quality of ethical review and motivation of REC members, since they might not be willing to be actively involved in a rather complex and time-consuming review process. As Dranseika and colleagues conclude regarding the situation in the Baltic States: “in general, the lack of motivators can both result in a poorer quality of ethical review and a reduction in the number of interested potential candidates” (Dranseika et al. 2011, p.53).

Ensuring transparency of the ethical review and providing training for REC members are problematic issues in CEE countries. For example, in Belarus, not a single REC, including the National Bioethics Committee (NBC), has its own website. In many cases, information on the REC procedures and functioning is not publicly available. With regard to the Baltic States, Dranseika and colleagues report the same: “very few RECs in the region have websites that provide information about their procedures. Information on statutes, de facto composition, basic statistics on the number of reviewed research protocols (not even including the list of approved and rejected research projects) in many cases is not publicly available” (Dranseika et al. 2011, p. 51). However, there are some positive examples coming from Lithuania, where several websites have recently been established that provide information about RECs. For example, the websites of the Lithuanian Bioethics Committee (LBC) and two regional committees contain the information on approved research projects, composition of RECs and legal acts that establish the operating procedures for the ethical review of biomedical research projects (official websites of the LBC, Kaunas and Vilnius RECs). In Poland, the information on the composition of RECs and some aspects of their activity can be found at the official websites of founding institutions (EUREC 2015).

With regard to training, there are no regular training programs for REC members in CEE countries. In fact, the only way for REC members to acquire some knowledge and skills on research ethics is through self-education and practical work on the committee (Dranseika et al. 2011). Some REC members participate in conferences or workshops, but this happens only occasionally. Again, there is a significant gap in providing important inputs to the program, as receiving adequate training is crucial for REC members to develop competence and the expertise needed to perform their functions properly.

Program management at the national level

According to the Strosberg and colleagues’ framework, the program for the protection of human research subjects is managed at the national level by organizations that oversee and support the entire system. Continuing with the analogy of an architect’s sketch of a building, these organizations are those who have to “turn the sketch into more detailed plans, construct the building, and maintain the building for the purpose for which it was constructed” (Strosberg et al. 2014, p.4). They are also supposed to undertake corrective actions if there is something wrong in the system structure and program performance. Therefore, in order to assess how the program is managed at the national level, organizations which are accountable for program performance should be identified. In order to get the

whole picture, it is important to identify reporting relationships among RECs and oversight agencies and what channels are used for information flow between them. Also, it cannot be taken for granted that coordinating organizations have sufficient capacity for performing their functions only because they are assigned to do so. Hence, whether these organizations are provided with appropriate tools to perform their functions and whether they actually use these tools are questions which need to be asked.

In CEE countries, the program management role at the national level is usually assigned to governmental agencies. Their functions may vary widely depending on jurisdictions, but for the most part, they are concerned with monitoring and inspection of RECs, as well as with sanctions in order to achieve compliance with regulations. However, their efficacy in accomplishing their tasks depends on the availability of adequate authority and resources.

For example, in Lithuania, the LBC supervises the rest of the committees and reviews their decisions upon appeal. Also, the LBC is supposed to provide consultation, education, and advocacy with regard to protecting human research subjects. The LBC plays an important role in overseeing of RECs' compliance with regulations through monitoring, inspection and sanctions. In Lithuania, the division of responsibilities and accountability between national and local bodies is clearly defined in key normative documents on research ethics. As a rule, serious violations of Good Clinical Practice rules, discovered by the Lithuanian State Drug Agency, are reported to the LBC, and sanctions on investigators are reported on the State Drug Agency website (Gefenas 2009).

In Belarus, there is also a central body involved in national-level program management - the National Bioethics Committee (NBC), which is accountable to the Ministry of Health. The NBC does not review research projects but works as a consultative body to the government and the public on bioethical issues and moral dilemmas related to medicine and biotechnology. The NBC is also charged with the task of coordinating and supervising local RECs, as well as developing training programs for REC members. However, the Decree of the Ministry of Health, which regulates activities of the NBC, lacks concrete mechanisms for putting the assigned functions into practice (Ministry of Health of the Republic of Belarus 2006). Issues of financial and administrative support for the Committee's work are not addressed in the document at all. Furthermore, for its more than seven years history there have been only sporadic activity, and not a single policy paper, opinion, or recommendation has been issued. It is possible to assume, therefore, that the NBC in Belarus exists only "on paper". As a result, local RECs are working without adequate coordination, technical help and methodological support.

The Central Medical Ethics Committee (CMEC) in Latvia occupies a central position in the national research ethics system, as it is supposed to coordinate and methodically supervise the operation of ethics committees reviewing biomedical research. Also, the CMEC conducts an ethical review of all types of research, except CDTs, and consults different sorts of institutions on issues of biomedical ethics. The CMEC is assigned with the tasks, among others, "to develop draft laws and other regulations regarding the ethics of biomedical progress" and "issue resolutions regarding research and biotechnologies of both national importance and international scale" (Silis 2010, p.60). However, despite having such an

extended mandate, in reality the CMEC is the weakest part of the system. In his analysis of the Latvian research ethics system, Silis (2010) concludes that because of the lack of budgetary and authoritative support, training and motivation of its members, the CMEC is not able to accomplish many of its assigned tasks.

In Poland, there is no central institution that oversees and monitors the performance of RECs. Some sort of coordination and control can theoretically be exercised at the local level by founding institutions, which in the case of Poland are medical universities, regional chambers of physicians and dentists and medical research centers (Waligora 2013). However, as there are no provisions for accountability in the regulatory documents, Polish RECs do not have any legal obligation to report on their work to higher authorities (Czarkowski and Rozanowski 2009). It appears that Poland lacks all the critical elements of program management, as there are no national mechanisms in place for “maintaining the building” and taking corrective actions in the case of appearance of deficiencies in REC performance. Waligora (2013) reported the results of two audits of REC practices, which have been conducted by the Supreme Audit Office of Poland. The auditors highlighted deficiencies at both national and institutional levels of program management, by pointing out failures of the national bodies to fulfill their oversight and management responsibilities, as well as failures of regional and local institutions to ensure follow-up responsibilities for individual RECs (Waligora 2013).

Policy dynamics and the impact of the post-communist transition

The analysis of research ethics systems in Belarus, Latvia, Lithuania and Poland has revealed substantial gaps in the relevant policies and major impediments to program performance. The most problematic areas in the systems reviewed relate to ensuring equal protection for human subjects participating in different types of research, managing conflict of interest in REC decision-making, maintaining transparency of ethical review and providing remuneration and training for REC members (Table 1). It appears that the countries in CEE share similar problems, although to varying degree. Together with common contextual features, these similarities suggest that there might be common roots of the problems identified. However, the analysis has revealed some differences among the countries as well, mostly in terms of approaches the countries use in addressing the problems mentioned above. Bearing this in mind, let’s look more closely at the conditions and wider socio-economic environment in which the research ethics systems of Belarus, Latvia, Lithuania and Poland have been developed.

In searching for the common ground, it would be helpful to remember that all the countries in CEE started to develop their research ethics systems “from scratch” about twenty years ago, just after obtaining independence at the end of the 1980s - beginning of the 1990s. At that time, newly sovereign countries desired an opportunity to become more integrated in the global context, including the areas of international science and technology. However, since the countries in CEE had no previous experience in establishing the protection of human research subjects, the general ideas concerning the structure and functions of research ethics systems were "imported" from Western countries and adapted to the local context.

By introducing ethical oversight of biomedical research, governments have assumed new functions and expanded the scope of their activities. However, this expansion has not been accompanied by strengthening of the institutional capacity to perform these new functions properly. This is an important point to note, as there is the distinction between the strength of state institutions and the scope of relevant functions. In setting out the significance of the institutional capacity, Francis Fukuyama draws attention to the difference between the two: "it … makes sense to distinguish between the scope of state activities, which refers to the different functions and goals taken on by governments, and the strength of state power – or the ability of states to plan and execute policies and to enforce laws clearly and transparently" (Fukuyama 2004, p. 7). It was the time of enormous socio-economic upheavals at the end of the 1980s - beginning of the 1990s, when the development of research ethics systems took place in CEE, and state institutions were rather weak. At that time, state institutions were only able to establish rather formal structures for ethical review in order to demonstrate that they could satisfy the procedural requirements of research sponsors. Thus, the gaps in the research ethics policies and programs in CEE might at least in part be the results of the imperfect balance between the strength of state institutions and the scope of their activities.

However, from that time research ethics systems of different countries in CEE and the countries themselves have developed differently. Initially, just after obtaining independence, Belarus, Latvia, Lithuania and Poland had more or less equal starting positions, as their political, economic and social models were quite similar. After a period of political turmoil it became clear that the Baltic countries and Poland chose a democratic way of development and integration with the EU, while Belarus retained a "soviet-like", authoritarian regime of governance. An important feature of authoritarianism is that it provides little opportunity for public participation and effectively prevents the processes of policy-making from being transparent and accountable. Adnan Ali Hyder and colleagues refer to these factors as unfavorable enabling conditions for the development of research ethics systems and those which negatively affect the capacity for protection of human research subjects (Hyder et al. 2009).

During the Soviet time, the authoritarian regimes in CEE relied heavily on a "top-down" approach in administering state functions, including those in the field of health care and biomedical research (Borovečki et al. 2005). In this case, implementation of policies is usually perceived as a largely technical process, where implementers are obliged to put policies into practice under the threat of sanctions. Also, the "top-down" approach is much more concerned with establishing formal structures and producing reports than bringing about real change. The logic of this approach is clearly seen in the implementation of research ethics policies in Belarus, with its lack of motivators for the front-line staff and ineffective management of the research ethics programs at local and national levels. Attributable to the "top-down" approach are also the low level of follow-up and responsiveness of the system, which are in place in the case of Belarus (Famenka 2011). The way research ethics policies and programs have been introduced in Belarus makes it possible to assume that national policy makers have been more concerned with creating favorable conditions for the pharmaceutical industry than with ensuring the protection of research

participants. This course of action has eventually resulted in the establishment of a quite dysfunctional system of ethical review, with profound gaps between rhetoric and reality.

In contrast, Latvia, Lithuania and Poland have chosen a democratic way of development and integration with the EU, which has substantially changed the structure and functions of the state institutions and, by implication, the national research ethics systems. Commitments to democratic principles of governance, respect of human rights, autonomy and dignity of human beings, added to widening the possibilities for the public to participate in decision-making, all have contributed to creating better enabling conditions for strengthening the protection of human research subjects in these countries. Although there are many problems in the area of research ethics, and they are to some extent similar to those identified in Belarus, it appears that the Baltic States and Poland address them in a quite different way. An approach they use in the implementation of research ethics policies and programs into practice corresponds to a “bottom-up” model. In contrast to the “top-down” approach, this model recognizes that front-line staff often play an important function in implementation, not just as executors of policy handed down from above, but as active participants in the whole process of policy-making (Buse et al. 2012). The examples of acknowledging such a role are the efforts undertaken in the Baltic States and aimed at enhancing REC independence by establishing regional models of ethical review, providing financial support to at least some RECs and enhancing transparency of ethical review by making the data of REC operations publicly accessible. The Polish example, which relates to audits of REC practices, highlights the role of enabling conditions in raising public awareness about the issue of inadequate protection of human research subjects. Although an audit conducted by an external body is a rather unusual form of assessment of REC performance, the example of Poland suggests that in a democratic society some sort of public control can be executed if internal mechanisms of self-assessment appear to be ineffective.

The need for enhancing the research ethics capacity in CEE

The substantial gaps in policies and major impediments to program performance which have been identified in the selected countries of CEE suggest that the capacity of research ethics systems in these countries might be inadequate to meet the emerging challenges of an increasingly globalizing biomedical research. At the time when transnational pharmaceutical corporations continue to move to the East and build up their presence in the region, local participants of multi-centre research are becoming the weakest part of the system. As national research ethics policies and programs lag behind the innovative marketing strategies employed by pharmaceutical companies, it appears that the countries of CEE are not ready to face the new challenges of globalization of biomedical research.

The substantial gaps in the scope and content of research ethics policies and major impediments to program performance in the selected countries of CEE show that the strength of state power in the field of research ethics is still insufficient to ensure adequate protection of human research subjects. Therefore, there is the need in CEE countries for strengthening the research ethics capacity through modification of relevant policies and improvement of program management.

In the process of policy modification, however, it should be remembered that, according to Fukuyama, “there is evidence that the strength of state institutions is more important in a broad sense than the scope of the state functions” (Fukuyama 2004, p. 19) and the focus should be on the plausibility and viability of appropriate policies and programs. From the perspective of the analytical model of the policy and program for the protection of research participants, it means that public policies on research ethics should be supported by adequate intellectual and material resources, which are needed for “translating” policies from paper to practice. These improvements can only be achieved through serious and sustained efforts aimed at enhancing the research ethics capacity through policy making, policy advocacy and program management.

An important aspect for policy modification in CEE is that the countries of the region (even neighboring ones, as in the case of Lithuania and Belarus) differ significantly in terms of functionality of their research ethics systems and the extent to which their public policies comply with international standards on research ethics. The level of protection of human research subjects varies from country to country and clearly depends on socio-economic and political factors of transition, as they are making up the enabling conditions for the development of research ethics systems. An important factor in the strength of a research ethics system is the membership in transnational organizations like the EU, as this membership implies the presence of democratic principles of governance and transparency in decision-making, as well as a high level of competence of those administering the functions of the state. As these factors are mostly absent in non-EU countries, there have emerged quite dysfunctional systems of ethical review with profound gaps in policies and programs for human subjects protection. The results of the study suggest that the countries of CEE might have different needs in terms of strengthening their research ethics capacity and this variety should be taken into account when planning capacity building efforts. The differences among the countries call for further research on the approaches which would work best to fill the gaps in policies and programs for ensuring effective protection of human research subjects.

Limitations of the Study

There are several limitations to this study. First, the scope of review has been limited to those CEE countries for which sufficient amount of information on their research ethics systems, policies and programs is available. There is but a little research on national research ethics systems has been conducted in the region, the majority of countries in CEE have not been covered by this review. Therefore, the group of countries chosen for the study might not be fully representative of the whole region, especially because of the wide variety of socio-economic and political characteristics among the countries in CEE. Until more research on national research ethics policies and programs in CEE are conducted, the study results can only be generalizable with caution. Second, the study has relied heavily on the results of previously conducted studies on national research ethics systems, and therefore might be prone to replicating a possible bias the investigators might have had in their research. Another limitation of the study relates to the kind of the information analyzed, which has been drawn from publicly available documents describing official policies and hence providing little data on their practical work. Although researchers acknowledge some

difficulties in accessing individual RECs because of the lack of transparency (Silis 2010; Famenka 2011), without the exact knowledge on how the implementation of policies and programs actually happens at the practical level the assessment of research ethics capacity in the selected CEE countries cannot be considered as completely objective. More research is needed to obtain knowledge on the day-to-day operations of RECs and their actual needs in terms of capacity building.

Conclusions

By applying the framework for assessment of the policy and program for human subjects protection to research ethics systems of the four CEE countries - Belarus, Latvia, Lithuania and Poland, substantial gaps in policies and major impediments to program performance have been identified, although to a varying degree. For the most part, public policies on the protection of human subjects reviewed lack consistency and mechanisms for their implementation. With regard to research ethics programs, they are not provided with the necessary “inputs”, such as adequate policy, organizational structure, administrative support, budget, training and transparency. In some cases, the stated goals of ensuring the protection of human research subjects remain only “on paper”, as the gaps between rhetoric and reality are too big to be filled without undertaking extensive and well-planned interventions.

An important finding of the study is that the level of protection of human research subjects in the CEE region varies from country to country and clearly depends on socio-economic and political factors of their transition. The differences identified suggest that the CEE countries might have different needs in terms of strengthening their research ethics capacity and therefore might require different strategies of policy making to promote research ethics in the region. Heterogeneity among the countries calls for further research on the approaches which would work best to fill the gaps in policies and programs for ensuring effective protection of human research subjects.

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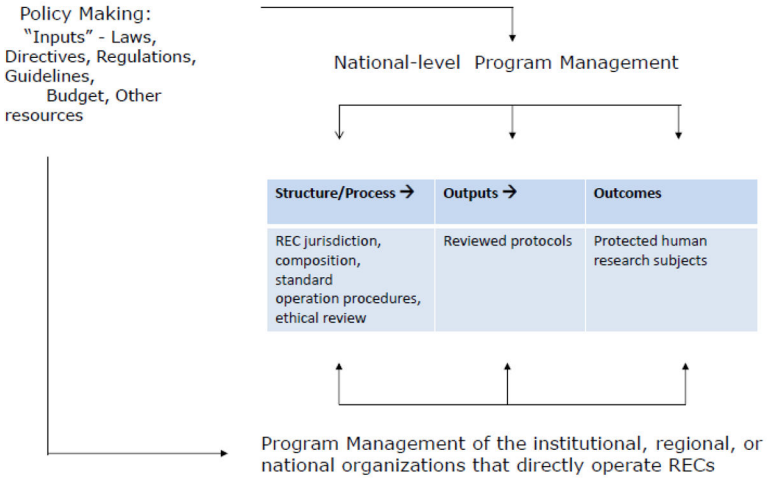

Fig. 1.

Policy and program for research ethics review. Adapted from Strosberg, Gefenas and Famenka (2014)

Table 1

Key characteristics and major gaps in the research ethics systems of the countries reviewed.

Features				
Country	**Belarus**	**Latvia**	**Lithuania**	**Poland**
Model of ethics review system	Institutional	Regional	Regional	
Central body of the system	National Bioethics Committee	Central Medical Ethics Committee	Lithuanian Bioethics Committee	N/A
Scope of ethical review	Narrow	Broad	Broad	Broad
Diversity of REC membership	Not ensured	Ensured	Ensured	Ensured
Administrative and financial support of RECs	Not ensured	Partly ensured	Partly ensured	Partly ensured
Transparency of a REC system	Not ensured	Partly ensured	Partly ensured	Partly ensured
Training for REC members	Not ensured	Partly ensured	Partly ensured	Partly ensured