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PERSPECTIVE

Ethics Review of Biomedical Research in Uzbekistan: Policy and Program Gaps

Dilfuza Aniyozova[1] · **Martin A. Strosberg**[2]

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Abstract
We describe the national health research ethics review system of Uzbekistan and identify policy and program gaps that impede the protection of human research subjects. We find that the National Ethic Committee (NEC), functioning at the national level, is solely responsible for conducting research ethics review. There is little evidence that regional ethics committees work as intended, and there is no research ethics review at medical institutes and research centers even though they conduct CDTs (clinical drug trials). There is no national policy for the ethical review of non-clinical trials. We recommend the establishment of institutional review boards (IRBs) at medical institutes and research centers while at the same time building capacity at the national level to oversee and support the research ethics review system of the entire country.

Keywords Research ethics · Ethics review · IRB · Biomedical research · Uzbekistan

Introduction

Uzbekistan, a Central Asian republic, with a population of more than 34 million, declared its independence from the Soviet Union in 1991 and underwent a major transformation of its economic and political systems. Like other transitions societies, Uzbekistan, attracted pharmaceutical companies, intent on conducting clinical drug trials in an increasingly commericialized healthcare system. To increase its attractiveness to and facilitate collaboration with pharmaceutical companies, Uzbekistan incorporated international research ethics standards into national law

✉ Dilfuza Aniyozova
adilfuza@gmail.com

[1] Tashkent Institute of Postgraduate Medical Education, Tashkent, Uzbekistan

[2] Clarkson University, Schenectady, NY, USA

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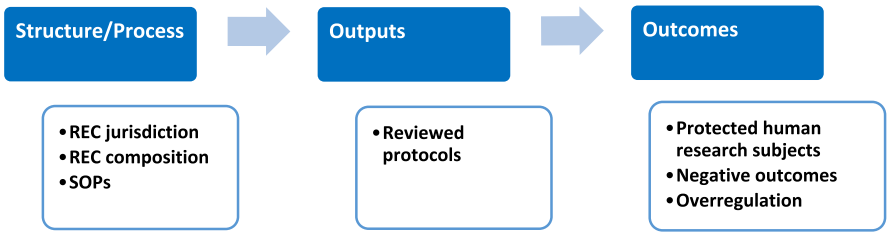

Fig. 1 Logic model of research ethics review

and regulation, including ICH Guideline for Good Clinical Practice[1] (Kubar 2010; ICH 1996). However, as Hyder et al. (2009) point out, programs instituted by the developing low-income countries to protect human research subjects are often defeated by constraints imposed by the larger socio-political environment.

In this article we presented the findings of the analysis of the research ethics review system of the Tashkent Institute of Postgraduate Medical Education and the national policies in Uzbekistan (constitutional, legal, regulatory guidelines) to identify the policy gaps and to develop the recommendations addressed for each level of the ethics review system to strengthen its capacity to protect human research participants.

Overview of Research Ethics Review System

To describe the research ethics review system of Uzbekistan and to identify policy and program gaps, we adopt the logic model as our analytical framework as depicted in Fig. 1. (Strosberg et al. 2014).

As will be explained, research ethics review, conceptualized in terms of structure/process, outputs, and outcomes, is carried out exclusively at the national level through the National Ethics Committee (NEC), which is guided by policies set forth by national law and international standards:

- The Law of the Republic of Uzbekistan, on the protection of citizens' health—permits to conduct biomedical research involving human subjects at state institutions after laboratory experiments and with informed consent from a research participant (Article 34) (Lex.Uz 1996).
- The Law of the Republic of Uzbekistan, on pharmaceutical products and pharmaceutical activity—protects patients' rights in biomedical research. It defines the State authorities and competence of the Ministry of Health (MoH) in the sphere of clinical trials (Article 10, 11) (Lex.Uz 2015).

[1] Guideline for Good Clinical Practice of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

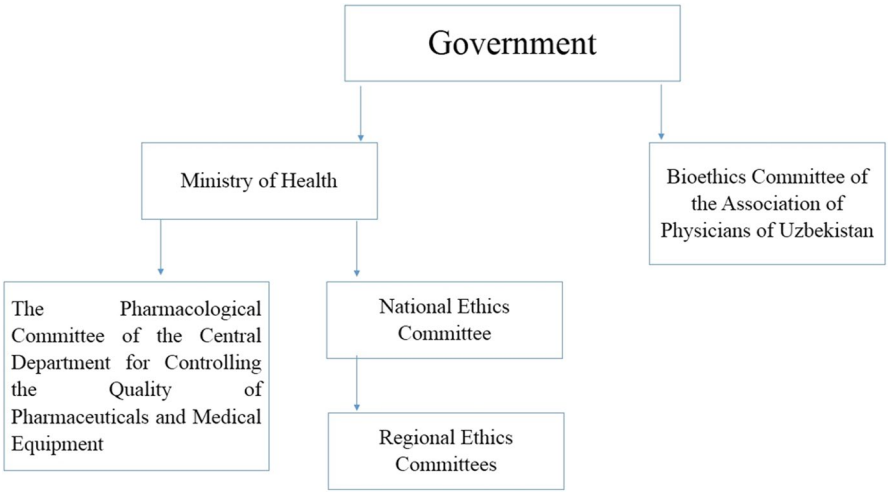

Fig. 2 Ethics review system in Uzbekistan

- WHO Guidelines for Good Clinical Practice, guidelines on conducting clinical trials and determining clinical sites—delineates requirements for informing patients about clinical trials, obtaining written informed consent, independent ethical review, and standard operating procedures (WHO 2018).
- The Ethical Code of Uzbekistan Physician-Investigator—sets out basic principles of ethical review of biomedical research involving human subjects[2] (MoH 2018).

The NEC is part of a larger organizational structure depicted in Fig. 2.

Accountable to the Ministry of Health (MoH), The Pharmacological Committee of the Central Department for controlling the quality of pharmaceuticals and medical equipment reviews preclinical studies and clinical drug trials (CDT) to assess for therapeutic effect, safety, and risks for research subjects in accordance with the GLP (Good Laboratory Practice) (Bank/WHO-TDR 2001) and GCP (Good Clinical Practice)[3] (Kubar 2010). If approved the protocol is sent to the NEC for final approval (Kubar 2010).

The NEC, also accountable to the Ministry of Health, has more than 25 members from different fields—medicine (clinical practitioners/physicians, scientists of the medical schools), pharmacology, biology, law, genetics, philosophy,

[2] The Ethical Code of Uzbekistan Physician-Investigator. Sets out basic principles of ethical review of biomedical research involving human subjects.

[3] Guidelines on Conducting Clinical Trials and Determining Clinical Sites." The Guidelines are based on WHO Guidelines for Good Clinical Practice and reflect the following aspects: informing patients about CT; obtaining written informed consent from patients; independent ethical review; operational standard procedures.

and representatives from the Ministry of Health, religious and public institutions, ombudsmen and the National Centre for Human Rights (Abdurakhmanova 2020).

The NEC is tasked with carrying out ethics and scientific review according to a set of standard operating procedures (SOPs) (Kubar 2010). Typically, protocols are reviewed within 7–30 days. If approved, researchers receive an official certificate of approval. The number of research protocols reviewed by NEC is increasing: 298 in 2018 and 347 in 2019 (Abdurakhmanova 2020). Since the COVID-19 pandemic, national and international research related to COVID-19 has increased. Within a 6-month period, 130 COVID-19 related research protocols were approved by NEC (Aniyozova and Abdurakhmanova 2020).

An official organization chart depicting the hierarchial reporting relationships among the components of Uzbekistan's research ethics review system would show four Regional Ethics Committees (RECs) reporting to the NEC (Kubar 2010). In theory, The Regional Ethics Committees are responsible for monitoring biomedical research approved by the NEC at the site of the research with regard to compliance with the review procedures, obtaining informed consent from the research subjects, research safety (serious adverse effects, inadequate reaction), and notifying NEC if the research should be terminated because of complications arising in the course of the biomedical research. Of course, a bold line on paper, connecting two organizational units at different hierarchical levels and thereby expressing their intended relationship, may in reality be quite thin or even nonexistent. In this case, it is non-existant. The Regional Ethics Committee component of the research ethics review system (to be located in the cities of Samarkand, Bukhara, Andijan, Nukus) has not yet been implemented.

The Bioethics Committee (BC) of the Association of Physicians of Uzbekistan is non-governmental organization and does not review research protocols. It consists of prominent physicians, many of whom are involved in scientific research. This Committee is an advisory rather than a policy making body. The BC activity includes publication of articles and abstracts related to actual issues of bioethics and medical ethics. The website of the Association of Physicians contains reports about BC's proceedings, conferences, and their participants (AVUZ 2020).

Policy and Program Gaps

The intention of Uzbekistan's national policy, as embodied in laws, regulations, and international guidelines, is the protection of human research subjects, as expressed as the outcome of our logic model. A national policy is like an architect's sketch for a building. Someone has to implement the policy—turn the sketch into a more detailed blueprint, construct the building, and maintain the building for the purpose which was constructed. In terms of our logic model, outcome is dependent on adequate structure and process. A reviewed and approved protocol does not constitute convincing evidence that research subjects will be protected.

We can consider the building as the "program"—the vehicle for accomplishing the objectives of the policy. As was stated earlier, the Regional Ethics Committee component of the program (i.e., building) has not yet been implemented nor

constructed. The NEC at this time is functioning as the single research ethics committee for the whole country. Based on limited, publicly available information, we believe that the budget, staffing, and training is not sufficient to effectively carry out its responsibilities. Included in those responsibilities is oversight of the entire research ethics review system much of which is still unconstructed.

The NEC members are working on a voluntary basis. NEC do not collect fees for review, and the Government provides funds only for NEC office supplies (Abdurakhmanova 2020). With regard to research ethics review competency, although members attended training sessions in the first decade of the century (Kubar 2010), there is no evidence that there has been any training in the last 12 years.

An important gap in national policy is the lack of requirement for review of non-CDT research. There is no national policy for ethical review of biomedical or non-biomedical research that is not related to clinical drug trials. Gefenas et al. (2010) argue that research projects imposing equal or similar risks and inconveniences on research participants should be subjected to equally stringent revew procedures. Clearly, this is not the case at the Tashkent Institute of Postgraduate Medical Education (TIPME (2022)), the leading scientific and educational center of the Ministry of Health of the Republic of Uzbekistan in the field of postgraduate training and retraining of medical workers (TIPME 2022). Although most research of its research involves CDTs, the number of non-CDTs is increasing. Non-CDTs, including psychological, sociological, and anthropolitical studies (some of which are carried out by PhD students), are reviewed by the TIPME's Scientific Board for methodological soundness, but are not reviewed by the NEC for the protection of human subjects.

Recommendations

In light of the above-mentioned policy and program gaps, we offer the following recommendations.

National Government of Uzbekistan

1. Passage of law and promulgation of appropriate regulations requiring ethical review for research involving non-clinical drug trials and non-clinical studies.
2. Passage of law and promulgation of appropriate regulations calling for abolishment of Regional Ethics Committees and establishment of Institutional Review Boards in their place to be located at medical schools and institutes (see details below).

NEC

3. Creation of an NEC webpage that will provide information on its mission, policies, membership, reports, forms, and templates. Regular updating and reporting on research ethics reviews will be a feature of this webpage.
4. Institution of regular training sessions for NEC members.

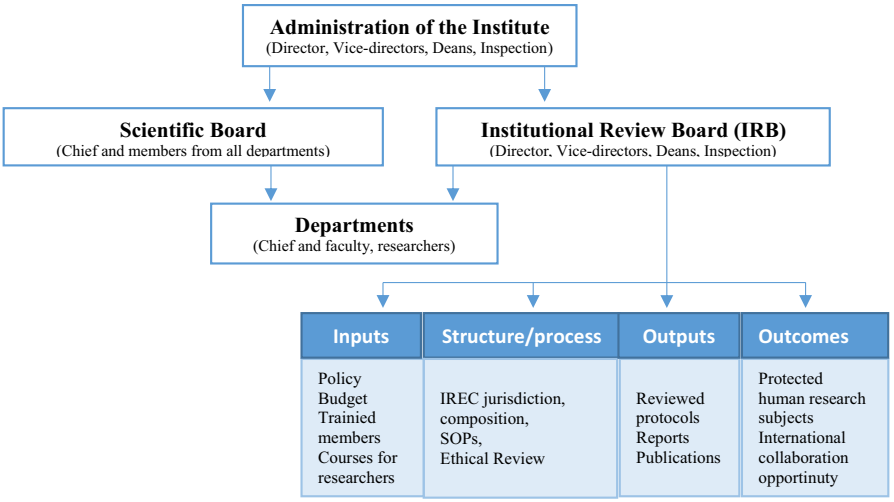

Fig. 3 Proposed model of IRB for TIPME

5. Re-emphasis of NEC's key role of manager of entire national research ethics review system to be composed of IRBs based at individual research institutes and universities (see below). NEC will review international research projects.

BC

6. Revision of the role of the Bioethics Committee of the Association of Physicians of Uzbekistan. BC will be responsible for capacity building through organization of training and re-training courses for NEC and IRB members. BC could establish relationship with International Bioethics Committee and invite international experts to the trainings for NEC members.

IRBs (Institutional Review Boards)

7. Establishment of IRBs (instead of Regional Ethics Committees) at the medical institutes (including TIPME) and national clinical research centers, where international and national research is conducted (Fig. 3). IRBs will be the key vehicle for the implementation of national policy on the protection of research participants involved in biomedical including non-clinical drug trials and non-clinical studies. IRBs will review only institutional studies.

The IRB will function according to a policy based on the Constitution of the Republic of Uzbekistan, the Law on protection citizens' health, adopted by Uzbekistan international guidelines related to research ethics, and research requirements of Ministry of Health of Uzbekistan and the institutes and centers. It will be under the auspices Scientific Board of the institutes and centers and with oversight by

Vice-directors. For example, the TIPME has a Scientific Board that responsible for approving all scientific research. Currently, the Board has 72 members, and it is chaired by the director of TIPME. Meetings of the Scientific Board of the Institute are held monthly. Its members review research protocols for methodological soundness. The proposed IRB will review research for the ethical protections of research subjects.

To carry out its research ethics review functions, IRBs will need trained IRB members, a budget, and policies including SOPs for CDT and non-CDT, guideline for submission of applications for the ethical review, informed consent templates, and conflicts of interest disclosure forms for its members. Like the NEC, the IRBs will maintain a public website describing its mission, criteria for appointing and selecting its chair and members, conflicts of interest disclosure, review procedures and methods for monitoring of the research, mechanisms for research participants' compliance, forms, templates, and regular reports on research review activity.

The Ethics Needs of Uzbekistan

8. Training of researchers in research ethics. Knowledge of the ethical aspects of research is mandatory among investigators to ensure that they have understood the principles of research that will help them to conduct research and report its results in appropriate way. Accordingly, researchers of all medical institutes and scientific centers should take a research ethics course as a basic course that will increase researchers' respect in scientific community, institution, and government. For instance, TIPME has an approved in 2016 by MoH short course in research ethics for PhD students. Training of NEC and IRB members should be organized by BC in collaboration with International Bioethics Committee.
9. Assessment of performance. NEC's and IRBs' performance can be measured externally and internally through an accreditation mechanism and using self-assessment tools (Sleem et al. 2010).

Conclusions

Our study shows that Uzbekistan has an incompletely implemented research ethics review system, operational only at the NEC level. Unfortunately, the regional ethics committees do not work. There is no research ethics review at medical institutes and research centers even though they conduct both CDTs and non-clinical trials. To protect research subjects and to meet current international requirements, there is an urgent need for Uzbekestan to establish a functioning research ethics review system relying primarily on the Institutional Review Boards at the medical institutes and national research centers. Conducting biomedical and non-biomedical research after ethical approval either by NEC or IRB will be basic requirement in ensuring human subjects' protection. Training of NEC and IRB members as well

as researchers should be compulsory to meet ethical principle in conducting and reviewing research projects.

Limitations of the Study

The findings of this study have to be seen in light of some limitations. We only analyzed publicly available data sources. We faced limited access to the NEC's internal policies and reports. We suggest conducting extensive interviews with NEC members and other governmental official.

Abbreviations *CDT*: clinical drug trial; *IRB*: Institutional Review Board; *NEC*: National Ethics Committee; *REC*: Research Ethics Committees; *SOP*: standard operational procedures; *TIPME*: Tashkent Institute of Postgraduate Medical Education; *WHO*: World Health Organization

Author Contributions Both authors contributed to the study conception and design. Data collection and analysis were performed by Dilfuza Aniyozova. Both authors commented on previous versions of the manuscript. Both authors read and approved the final manuscript.

Data Availability Not applicable.

Declarations

Ethics Approval This is a qualitative research/policy analysis. The study did not require an ethical approval.

Competing Interests The authors declare no competing interests.

Consent Not applicable.

References

Abdurakhmanova, N. 2020. Face to face interview on structure, composition of NEC of Uzbekistan.

Aniyozova, D., and N. Abdurakhmanova. 2020. The current issues of ethical review system in Uzbekistan in the context of Covid-19. In *Online presentation at the International Conference "Ethical and Regulatory issues of health research, including clinical trials in the context of pandemic Covid-19" November 27, 2020*. Astana Kazakhstan.

AVUZ. 2020. Bioethics Committee of the Association of Physicians of Uzbekistan. 2020. http://www.avuz.uz/history-bioethics. Accessed 20 June 2023.

Gefenas, E., V. Dranseika, A. Cekanauskaite, et al. 2010. Non-equivalent stringency of ethical review in the baltic states: a sign of a systematic problem in Europe? *Journal of Medical Ethics* 9: 435–439. https://doi.org/10.1136/jme.2009.035030.

Hyder, A., L. Dawson, M. Bachani, et al. 2009. Moving from research ethics review to research ethics systems in low-income and middle-income countries. *Lancet* 373: 862–865. https://doi.org/10.1016/s0140-6736(09)60488-8.

ICH. International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. 1996. Guideline for Good Clinical Practice. https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf. Accessed 20 June 2023.

Kubar, O. 2010. *The current state of bioethics education in the system of medical education in the CIS member states*, 24–32. Saint Petersburg: Pasteur Institute https://unesdoc.unesco.org/ark:/48223/pf0000187351. Accessed 20 June 2023.

Lex.U. 1996. The law of the Republic of Uzbekistan on the protection of citizens' health of 1996. https://lex.uz/acts/41329. Accessed 20 June 2023.

Lex.U. 2015. The law of the Republic of Uzbekistan on pharmaceutical products and pharmaceutical activity of 2015. https://www.lex.uz/acts/2856466. Accessed 20 June 2023.

MoH. 2018. The ethical code of Uzbekistan physician-investigator. https://nrm.uz/contentf?doc=109828_prikaz_ministra_zdravoohraneniya_ot_25_07_2001_g_n_334_ob_usovershenstvovanii_provedeniya_klinicheskih_ispytaniy_lekarstvennyh_sredstv&products=1_zakonodatelstvo_respubliki_uzbekistan

Sleem, H., R. Abdelhai, I. Al-Abdallat, et al. 2010. Development of an accessible self-assessment tool for research ethics committees in developing countries. *Journal of Empirical Research on Human Research Ethics* 5 (3): 85–98. https://doi.org/10.1525/jer.2010.5.3.85.

Strosberg, M., E. Gefenas, and A. Famenka. 2014. Research ethics review: identifying public policy and program gaps. *Journal of Empirical Research in Human Research Ethics* 2: 3–11. https://doi.org/10.1525/2Fjer.2014.9.2.3.

Tashkent Institute of Postgraduate Medical Education. 2022. https://tipme.uz/uz/page/1. Accessed 20 June 2023.

UNDP/World Bank/WHO-TDR. 2001. Good laboratory practice of 2001. https://tdr.who.int/publications/m/item/2001-01-01-handbook-good-laboratory-practice. Accessed 20 June 2023.

WHO: Guidelines for Good Clinical Practice. 2018. Handbook for good clinical research practice (GCP): guidance for implementation. https://extranet.who.int/pqweb/sites/default/files/documents/GCP_handbook_1.pdf.