

HemCenter LLP

APPROVED by Order of the Director General
of HemCenter LLP No. I-02-44 dated 31 May 2023

**REGULATION
ON THE LOCAL BIOETHICS COMMITTEE OF HEMCENTER LLP**

1. General Provisions

- 1.1. This Regulation defines the functions and powers of the Local Bioethics Committee (hereinafter – the LEC) of HemCenter LLP (hereinafter – the Center) and has been developed in accordance with the legislation of the Republic of Kazakhstan and the internal documents of the Center.
- 1.2. The LEC is an independent expert body of the Center composed of leading scientific specialists and representatives of public organizations who protect the rights, safety and well-being of trial subjects and investigators and carry out the ethical, moral and legal assessment of clinical trial/study materials where disputed issues arise at any stage of a clinical trial/study, as well as after its completion.
- 1.3. In its work the LEC is guided by: the Constitution of the Republic of Kazakhstan, the Code of the Republic of Kazakhstan "On Public Health and the Healthcare System", the laws of the Republic of Kazakhstan, the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986); the Convention on Human Rights and Biomedicine (1997); the Declaration of Helsinki, the World Health Organization guidelines for ethics committees that review biomedical research (2000); the Good Clinical Practice (GCP) Standard, this Regulation and other sector-specific regulatory documents.

2. Purpose, Tasks and Functions of the Local Bioethics Committee

- 2.1. **The main objectives** of the Local Bioethics Committee of HemCenter LLP (hereinafter – the LEC) are the independent review of the ethical aspects of clinical and scientific studies involving patients as trial subjects, the protection of their health, rights and interests, the establishment of guarantees of their safety and compliance with ethical standards, as well as other matters related to compliance with the rules of medical practice and research ethics.
- 2.2. **The tasks of the LEC** are
 - 2.2.1. objective, independent assessment of the relative risks and benefits and of the safety of the materials of clinical trials involving new technologies, medicinal products, food supplements, medical equipment, medical devices and new methods of treatment, in compliance with humanistic and ethical principles and legal norms in respect of trial subjects (patients), both at the planning stage and during the conduct of the study;
 - 2.2.2. assessment of the compliance of the clinical trial programme with the standards of good clinical and scientific practice (GCP), as well as with the qualifications of the investigators and the technical equipment of the healthcare organization conducting the study;
 - 2.2.3. assessment of compliance with international and national ethical standards in the conduct of biomedical research
 - 2.2.4. participation in the development of documents on bioethics issues in the conduct of research at the local and national levels.
- 2.3. **The functions of the LEC** are
 - 2.3.1. determining the advisability of conducting each study submitted to the LEC for review;
 - 2.3.2. conducting ethical review of draft scientific and technical programmes of an applied and fundamental nature, irrespective of the sources of funding, and of the performance of scientific research that has been awarded grants;
 - 2.3.3. regular monitoring of the study process after the LEC has granted permission to conduct it;
 - 2.3.4. review of interim and final reports on clinical trials previously approved by the LEC;
 - 2.3.5. review of cases of non-compliance with ethical principles in scientific publications and projects where breaches of intellectual integrity, falsification, plagiarism or false co-authorship are detected;
 - 2.3.6. review of matters concerning the ethical aspects of medical practice, as well as matters related to the rights and safety of patients;
 - 2.3.7. review and resolution of conflicts of interest between investigators and study subjects;
 - 2.3.8. review of information (reports) on adverse reactions and adverse events in clinical trials, of medicinal products and of medical devices;

- 2.3.9. review and approval of the Center's standard operating procedures with regard to ethical appropriateness and patient safety.

3. Scope of Activity of the LEC

- 3.1. The LEC conducts an ethical review of every study involving human participants before it begins, and also ensures regular follow-up monitoring of compliance with ethical principles in the course of the study and after its completion.
- 3.2. The LEC is responsible for the ethical review and oversight of all biomedical research conducted in this organization, including scientific research conducted by non-affiliated investigators from other organizations.
- 3.3. Types of biomedical research subject to review by the LEC:
 - 3.3.1. clinical trials of medicinal products, medical devices and medical equipment;
 - 3.3.2. epidemiological studies;
 - 3.3.3. sociological studies;
 - 3.3.4. studies involving medical records or personal data;
 - 3.3.5. studies involving biological samples;
 - 3.3.6. health systems research;
 - 3.3.7. implementation research.

4. Structure and Composition of the LEC

- 4.1. The structure of the LEC is approved by Order of the Director General of the Center.
- 4.2. The LEC may comprise up to 11 members, but not fewer than 5 (excluding the Secretariat). Gender balance must be maintained in the composition of the LEC, and it must include:
 - 4.2.1. persons who collectively have the qualifications and experience to review and evaluate the scientific, medical and ethical aspects of the proposed study;
 - 4.2.2. a member whose area of expertise is not scientific research;
 - 4.2.3. a specialist who is not an employee of the medical organization or clinical site where the study is conducted (a non-affiliated member);
 - 4.2.4. representatives of the public (lawyers, public organizations, etc.).
- 4.3. LEC members act not as representatives of the organization that is their principal place of employment, but as independent experts.
- 4.4. Persons who are part of the Center's management may not be LEC members, given that the LEC (and its decisions) must be independent of the management and governing bodies of the Center in order to avoid conflicts of interest.
- 4.5. LEC members are elected for a term of 3 (three) years with the possibility of re-election for a subsequent term.
 - 4.5.1. at the end of an LEC member's term of office, the LEC may offer the member reappointment for a new three-year term, provided that the person continues to meet all the necessary qualification requirements;
 - 4.5.2. reappointments are confirmed by an extract from the LEC meeting minutes and by an Order of the Director General of the Center no later than the date of expiry of the LEC member's term of office.
 - 4.5.3. the number of reappointments of a member is not limited.
- 4.6. The LEC must carry out a partial rotation after the three-year period of membership.
- 4.7. Expansion of the membership and the admission of new members are carried out by decision of the LEC Chair.
 - 4.7.1. new members are admitted to the LEC after their candidacies have been approved by the LEC members;
 - 4.7.2. the LEC Chair prepares the discussion of candidacies: surveys all LEC members regarding their intention to include the candidates, obtains from them information on the consent of the named candidates, or

- from the candidates themselves on their possible inclusion in the LEC, and requests a professional curriculum vitae from the candidates.
- 4.7.3. the LEC Chair may independently take a decision on the selection of a candidate for the LEC, provided that an atmosphere of mutual respect and trust and of goodwill is ensured and that conflict situations are prevented in the ethical review of clinical trials where the opinions of LEC members differ;
 - 4.7.4. the discussion of candidacies is conducted on the basis of the recommendation of the LEC member who proposed the candidate and of the candidate's professional curriculum vitae. A condition for the discussion is the candidate's consent to possible inclusion in the LEC, to comply with GCP rules, to follow the standard operating procedures (SOPs) of the LEC and to sign a confidentiality undertaking. One or more LEC members may hold a confidential interview with the candidate to clarify questions that arose during the discussion;
 - 4.7.5. the LEC decision to approve a candidate is taken by consensus at an LEC meeting. After the new LEC members have been approved, the Chair enters and approves the corresponding addition to the LEC membership list, indicating the date of the addition;
 - 4.7.6. upon joining the LEC, each participant must sign a confidentiality agreement ensuring that information not subject to disclosure is kept secret from persons not authorized to receive it. LEC members must declare any conflict of interest they may have or any degree of interest – financial, professional or otherwise – in any project or proposal subject to review, and the LEC must determine whether, and on what conditions, LEC members who have any conflict of interest may take part in the discussion and in the formulation of the LEC's recommendations.
- 4.8. LEC members may withdraw from the LEC before the expiry of their term of office by submitting a letter of resignation to the LEC Chair, in the event of:
 - a decision by the member to resign voluntarily; transfer to other employment that is incompatible with his or her role in the LEC.
 - 4.9. LEC members may be removed from the LEC by decision of the remaining LEC members for improper performance of their duties: evasion of participation in meetings, disclosure of confidential information concerning a specific clinical trial and/or the proceedings of LEC meetings, systematic (more than 1/3 of decisions per year) refusal to take part in decision-making owing to a conflict of interest; disrespectful treatment of colleagues; abuse of their powers.
 - 4.10. The activities of the LEC are carried out by the Chair, the Deputy Chair, the members and the Secretariat of the LEC.
 - 4.10.1. **LEC Chair**
 - 4.10.1.1. A person appointed to the position of LEC Chair must meet certain qualification requirements (length of service, experience of work in the LEC, completed training in research ethics, etc.).
 - 4.10.1.2. Duties of the LEC Chair exercises overall management of the activities of the LEC; draws up the LEC work plan, as well as the agenda of a regular or extraordinary meeting of the LEC conducts LEC meetings; appoints a reviewer from among the LEC members to carry out a preliminary review of the proposed study; in disputed cases and in other circumstances where a proper review cannot be carried out by the LEC members themselves, engages an independent expert who is not an LEC member; develops proposals, additions and changes concerning the activities of the LEC and submits them for discussion by the LEC members; provides clarifications to interested parties on the activities of the LEC and the grounds for LEC decisions.
 - 4.10.2. **LEC Deputy Chair:**
 - exercises the powers of the LEC Chair during the Chair's absence, as well as during the review of a proposed study in which the LEC Chair is an investigator;
 - performs other functions as instructed by the LEC Chair.
 - 4.10.3. LEC members:

- attend LEC meetings;
- review, discuss and appraise proposals concerning studies submitted for expert evaluation; review reports on the progress of studies and on changes and additions to the study protocol and the voluntary informed consent form, and monitor ongoing studies;
- review reports upon completion of studies;
- declare any conflict of interest when conducting the ethical review of a study;
- ensure the confidentiality of documents and of their discussion at meetings.

4.10.4. LEC Secretariat:

4.10.4.1. The LEC Secretariat is the coordination centre for all matters related to the work of the LEC.

4.10.4.2. The tasks and duties of the LEC Secretariat include:

- informing and advising investigators, sponsors and new LEC members on the applicable rules, instructions, processes and procedures;

- ensuring the timely progress of the review of study documents, including assisting investigators in preparing the application, in ensuring the completeness of applications and in preparing the file for submission to the LEC for review;

- maintaining regular contact with investigators in order to provide information on the review process and the status of their application;

- preparing for LEC meetings, including distributing the relevant documents to members, scheduling and ensuring a quorum;

- following up on the tasks that the LEC assigns to Principal Investigators, such as progress reports, final reports, corrective actions, amendments to the approved protocol or approval documents, etc.;

- preparing, in close cooperation with the Chair, reports on Committee meetings and annual reports on the activities of the LEC;

- maintaining records, including the study protocols and all correspondence related to their review, as well as periodic reports on the progress of a study after its approval. The Secretariat ensures that the confidentiality of LEC documents is preserved.

4.10.4.3. The Secretariat is managed by

the Chair and is elected by the LEC members for 3 years, and may subsequently be re-elected.

4.10.4.4. The number of staff of the LEC Secretariat is determined on the basis of the workload:

- 1 (one) staff member: where no more than 50 study protocols are reviewed annually;

- 2 (two) staff members: where no more than 150 study protocols are reviewed annually;

- 3 (three) staff members: where no more than 250 study protocols are reviewed annually.

4.10.4.5. The LEC Secretariat may be disqualified by decision of the LEC where there are appropriate grounds, and this is done by a vote of the LEC members.

4.10.4.6. The LEC Secretariat may resign from office at its own request by submitting a letter of resignation to the LEC Chair.

4.10.5. LEC Secretary

- ensures liaison between the investigator and the LEC; receives and registers documents submitted to the LEC;

- carries out a preliminary assessment of the completeness and correct execution of the submitted documents and, where deficiencies in the execution of documents or the absence of required documents are identified, notifies the investigator thereof;

- agrees the date of a regular or extraordinary meeting with the Chair and communicates it, together with the agenda, to the LEC members and other invited persons;

- keeps the minutes of the LEC meeting;

- monitors the timely submission by investigators of reports on ongoing studies, as well as of the report upon completion of a study;

where an investigator fails to submit a report within the established time limit, promptly informs the LEC Chair thereof;

prepares and archives all necessary documentation (documents submitted to the LEC by the investigator, meeting minutes, document templates);

4.10.6. Independent Consultants of the LEC:

An independent consultant may be appointed by the LEC Chair from among experts in highly specialized disciplines or issues to carry out the review of a specific study.

- 4.11. The activities of the members are governed by this LEC Regulation and by the job descriptions and standard operating procedures of the LEC.

5. Management of LEC Activities

- 5.1. The activities of the LEC are governed by the Regulation on the LEC and by the standard operating procedures (SOPs) approved by the LEC Chair.
- 5.2. SOPs are reviewed every 3 (three) years and are also amended as necessary. The LEC regulates the process of documenting/retaining all previous versions.
- 5.3. The Regulation and SOPs of the LEC must be provided at the request of investigators or study sponsors and must be publicly available, in particular posted on the organization's website.

6. Rules of Procedure of the Committee

- 6.1. LEC meetings are held in accordance with the established schedule and/or as necessary and are deemed quorate if at least 2/3 of its members are present;
- 6.2. LEC members participating in the proposed clinical trial are not involved in the discussion of the submitted clinical trial materials and are not permitted to vote;
- 6.3. All members of the Committee and the Secretariat must treat any information received by the LEC as confidential. The Committee's deliberations and discussions are confidential; therefore, Committee members must not discuss with other persons what was said about a specific project or investigator during a meeting, unless permission to do so has been given.
- 6.4. Independent consultants and external experts must also maintain the confidentiality of information. Best practice is to use official channels of communication between the LEC (the Chair and the Secretariat) and investigators, the administration of the organization and other partners.
- 6.5. LEC decisions are taken by a simple majority of votes of the Committee members by open voting, provided there is a quorum, and are recorded in minutes. Each LEC member has one vote. The right to vote may not be transferred to other persons. In the event of a tie, the LEC Chair has the casting vote. Meeting minutes and LEC recommendations are signed by the Chair and the Secretary of the LEC;
- 6.6. All documents must be stored in accordance with a procedure that ensures their safekeeping and confidentiality.

paper documents should be kept in lockable filing cabinets to which only the Secretariat and the LEC have access. They must be located in a dedicated Secretariat office, which is also kept locked.

electronic documents must be stored in systems with restricted access. Any files containing information that could identify study participants should also be password-protected.

- 6.7. It is recommended that documents be retained for 3 years after completion of the study and that all files then be securely destroyed with the permission of the Principal Investigator for each study.
- 6.8. The LEC maintains and retains the necessary documentation (standard procedures, lists of Committee members, meeting minutes, materials of clinical trials of medicinal products, reports, etc.) in accordance with the records management procedure adopted at the Center.

7. Rights and Obligations of the Committee.

- 7.1. The Committee is entitled to:

- 1) request from the customer any information regarding a clinical trial or study, a preclinical (non-clinical) trial (study), and additional details of the study or trial if, in the opinion of the LEC, this information would substantially enhance the protection of the rights, safety and/or well-being of trial subjects;
- 2) seek assistance from other independent experts and consultants who are specialists in various fields;
- 3) give clarifications, recommendations and instructions and take decisions on matters within its competence;
- 4) the inadmissibility of enrolling a trial subject in a study or trial before the LEC has issued a written opinion on its conduct with regard to the disputed issues that have arisen;
- 5) documenting the activities of the LEC, determining the procedure for meetings, keeping meeting minutes, notifying its members of forthcoming meetings, and organizing meetings.
- 6) the proper and timely performance of the functions provided for by this Regulation;
- 7) organizing the activities of the LEC in performing the tasks and functions assigned to it

8. Administrative Support of the LEC

- 8.1. The Center provides the LEC with sufficient funding for its effective functioning:
 - 8.1.1. office premises with the necessary equipment;
 - 8.1.2. professional development and continuing education;
 - 8.1.3. stationery and office equipment;
- 8.2. The administrative expenses of the LEC may be covered by way of reimbursement from bioethical review conducted on a contractual basis, as well as from the Center's own funds.

9. Independence and confidentiality of the LEC's activities

- 9.1. The LEC and its decisions shall be independent of political, institutional, professional, financial or other relationships.
- 9.2. Organizations, investigators and sponsors should refrain from interfering in the review process or otherwise exerting pressure on committee members. Interference includes offering remuneration to a member who reviews a research project, or threatening consequences should the LEC not approve the project.
- 9.3. Executives and administrative staff shall not serve as LEC members or attend its meetings as observers.
- 9.4. All LEC members and the Secretariat shall treat any information received by the LEC as confidential. The committee's deliberations and discussions are confidential; therefore, committee members shall not discuss with other persons what was said about a specific project or investigator during a meeting, unless permission to do so has been given. Independent consultants and external experts shall also maintain the confidentiality of information.
- 9.5. The Chair, LEC members and independent consultants sign an agreement on the absence of a conflict of interest before commencing work in the LEC. A conflict of interest arises whenever a member's duties and obligations to the LEC come into conflict with other interests, whether personal, professional or financial.
- 9.6. LEC members who have a conflict of interest with specific studies for any reason shall declare this before the meeting begins and shall recuse themselves, or be recused, from any discussion or decision-making related to that project. If an LEC member does not participate because of a conflict of interest, the quorum of the committee meeting must still be ensured.

10. Professional training and continuing education of LEC members

- 10.1. The organization is responsible for ensuring appropriate training of LEC members, who shall receive professional and continuing education in the ethical review of biomedical research and related fields on a regular basis.
- 10.2. The Chair and the Secretariat of the LEC develop a training plan and submit an application for the LEC budget to include the costs of training and professional development of the Chair and LEC members.

11. Reporting on the LEC's activities

- 11.1. The LEC is accountable to the management of the Center.
- 11.2. The Chair of the LEC shall submit an annual report to the management of the Center, as well as a yearly report to the Central Bioethics Commission of the Ministry of Health of the Republic of Kazakhstan by 30 November of the current year.

12. Interaction with other bioethics committees

- 12.1. Interaction with other local bioethics committees
 - 12.1.1. Multicenter studies conducted at several centers/sites may require review by several LECs, since each LEC must subject to ethical review all research projects conducted at the Center. The Center may enter into bilateral agreements with other organizations for the mutual recognition of LEC review (the approval of the LEC of one organization is accepted by the second organization without the need for review by the second organization, but with registration in both).
 - 12.1.2. A formal memorandum of understanding setting out the policy and procedures for the mutual recognition of LEC review covers such matters as:
 - the names of the participating LECs and a clear statement that the review of one LEC will be accepted by the participating LECs and vice versa;
 - the local recognition procedure (standard operating procedures, templates, etc.);
 - the reporting structure for the annual review of project status, and the requirements for immediate reporting and project completion.
 - 12.1.3. The matter of interaction with other LECs shall be coordinated by the LEC Secretariat in each organization
- 12.2. Interaction with the Central Bioethics Commission of the Ministry of Health of the Republic of Kazakhstan
 - 12.2.1. The mechanism of interaction between the LEC and the Central Bioethics Commission of the Ministry of Health of the RK shall be described in a formal memorandum of understanding,
 - 12.2.2. The Central Bioethics Commission of the Ministry of Health of the RK applies the same standard working procedures, with certain exceptions related to interaction with the authorized body.
 - 12.2.3. . Based on the results of their activities, LECs annually submit to the Central Bioethics Commission of the Ministry of Health of the RK a report on the work performed by 30 November of the reporting period.

13. Legal framework

- 11.1. In its activities, the LEC is guided by:
 - 13.1.1. the Constitution of the Republic of Kazakhstan of 30 August 1995;
 - 13.1.2. the Code of the Republic of Kazakhstan "On Public Health and the Healthcare System" of 18 September 2009;
 - 13.1.3. the State Standards of the Republic of Kazakhstan "Good Laboratory Practice" and "Good Clinical Practice", approved by Order of the Minister of Healthcare and Social Development of the Republic of Kazakhstan No. 392 of 27 May 2015 "On Approval of Good Pharmaceutical Practices";
 - 13.1.4. other regulatory legal acts of the Republic of Kazakhstan governing clinical trials;
 - 13.1.5. the Declaration of Helsinki of the World Medical Association;
 - 13.1.6. the Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, World Health Organization (2011);
 - 13.1.7. other international declarations and guidelines in the field of research ethics (WHO, ICH-GCP, UNESCO, CIOMS, CE); 8) the Regulation on the Local Bioethics Committee.