

Document type	SOP (Standard Operating Procedure)					
Intended for	Chair, Secretary and members of the Local Bioethics Committee of HemCenter LLP					
Nomenclature code	I-05	Number	Issl-3-6	Revision	001	
Title	INITIAL REVIEW OF RESEARCH DOCUMENTATION (APPLICATIONS, STUDY PROTOCOLS)					
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Agreed by	Medical Director		Klodzinskiy A.A.		29 May 2023	
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Approved	By Order of the Director General of HemCenter LLP No. I-02-52 dated 2 June 2023					
Implemented						
Revision policy	Upon changes in regulatory legal acts and/or operational need					

Purpose

To establish the procedure for the initial consideration of submitted applications and the compliance of a planned biomedical study, including a clinical trial of a medicinal product and other medical technology, with the established ethical requirements of the Local Bioethics Committee of HemCenter LLP

Responsibilities

The members of the Local Bioethics Committee of HemCenter LLP (LEC), or independent consultants, are responsible for thoroughly reviewing the documents (study protocol, etc.), completing the assessment form and communicating their decision, observations and comments within the established time limits.

The LEC Chair is responsible for appointing a reviewer from among the LEC members or independent consultants to conduct the review, and for the decision to include consideration of the study in the agenda of the current LEC meeting.

The LEC Secretary is responsible for receiving, checking and managing the document package in electronic and paper form. In addition, the LEC Secretary must compile a special package containing the study documents, distribute the packages to the LEC members for review and notify the applicant of its results.

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No. Terms and definitions

- a. **Biological equivalence** (hereinafter – bioequivalence) – the absence of significant differences in the rate and extent to which the active substance or active moiety of pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of its action when administered at the same molar dose under similar conditions in an appropriately designed study
- a. **Investigator's Brochure** - a compilation of the results of the clinical and preclinical (non-clinical) study of the investigational product that are relevant to its study in humans.
- b. **State expert organization in the field of circulation of medicinal products and medical devices** (hereinafter – the expert organization) – a state monopoly entity carrying out production and economic activities in the field of healthcare to ensure the safety, efficacy and quality of medicinal products and medical devices.

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- c. **Study design** - the overall plan of the study, a description of the manner in which the study is conducted depending on the selection and formation of groups of study subjects and the blinding (masking) of data.
- d. **Contract** - a dated and signed agreement between two or more parties that sets out arrangements concerning the allocation of the scope of work and responsibilities in the conduct of a study and, where necessary, financial matters. The study protocol should serve as the basis of the contract.
- e. **Case report form** - a document on paper, electronic or optical media designed to record all the information required by the protocol to be reported to the sponsor on each study subject.
- f. **Interventional study** – a study involving a human as a study subject, in which the investigator-physician, on the basis of an interventional clinical trial protocol that complies with the procedure for conducting clinical trials, assigns a specific intervention to the study subjects.
- g. **Informed consent** - a procedure by which a study subject or his or her legal representative voluntarily confirms consent to participate in a particular study after having been informed of all aspects of the study that are relevant to the decision. Written informed consent is documented using the form approved by the authorized body.
- h. **Bioequivalence study** – a comparative study of bioavailability aimed at establishing pharmacokinetic equivalence between the test product and the comparator product.
- i. **Investigator** - an individual responsible for the conduct of a clinical trial at the clinical sites of HemCenter LLP, a member of the research team.

Where a study is conducted at a clinical site by a group of investigators, a **Principal Investigator** - the head of the research team - is designated. The Principal Investigator is selected by the members of the Clinical Project Office and approved by the Director General of HemCenter LLP. The Order appointing the members of the research team (investigators) is approved by the directors of the branches and the division of HemCenter LLP

- j. **Investigational product** - a pharmaceutical form of an active substance or placebo being tested or used as a control in a clinical trial, including an authorised medicinal product where it is used in a way different from the approved one, or when used for a new indication or to gain further information about an approved indication
- k. **Ethics committee** - a consultative and advisory body established at the national level (the Central Bioethics Commission) and at the level of a medical organization, composed of specialists in healthcare and science and representatives of public organizations, which protects the rights, safety and well-being of study subjects and investigators and carries out the ethical and moral-legal assessment of clinical trial materials.

Local Bioethics Committee (LEC) of HemCenter LLP - an independent body that protects the rights, safety and well-being of patients, trial subjects, investigators and healthcare workers and carries out the ethical and moral-legal assessment of materials related to medical and scientific activities.

- l. **Clinical site** - a healthcare organization that conducts clinical trials.
- m. **Clinical trial** - a study involving a human as a subject, conducted to identify or confirm the safety and efficacy of means, methods and technologies for the prevention, diagnosis and treatment of diseases.
- n. **Contract research organization (CRO, Contract research organization)** — an individual/organization that, under a contract with the sponsor, performs one or more of the sponsor's functions related to the conduct of a clinical trial.
- o. **Confidentiality** - keeping information belonging to the sponsor, or information that makes it possible to identify a study subject, secret from unauthorized persons. Materials containing restricted information.
- p. **Medicinal product** – a product that is or contains a substance or combination of substances that comes into contact with the human body and is intended for the treatment or prevention of human diseases, or for restoring, correcting or modifying human physiological functions by exerting a pharmacological, immunological or metabolic action, or for the diagnosis of human diseases and conditions.
- q. **Study materials** – a set of documents submitted by the sponsor of clinical trials to the clinical site, which includes the authorization of the authorized body in the field of healthcare of the Republic of Kazakhstan to conduct the given clinical trial and to designate those responsible for its conduct in accordance with the procedure approved in the Republic of Kazakhstan; the clinical trial protocol; the Investigator's Brochure;

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explanatory documents on the specifics of the use of new medical technologies (where used) and other documents, as well as the draft clinical trial contract

- r. **Medical record** — a medical document in which the attending physicians record the patient's medical history (inpatient or outpatient) and the treatment prescribed to the patient, in electronic or paper form.
- s. **Multicenter clinical trial** - a clinical trial conducted according to a single protocol at more than one study center and by more than one investigator.
- t. **Clinical trial monitor** – an individual appointed by the sponsor or contract research organization who works together with the coordinating investigator or coordinating committee and oversees the conduct of the clinical trial in accordance with the protocol, assesses the degree of its implementation, and assists the investigator in the analysis, interpretation and extrapolation of data.
- u. **Monitoring** - the procedure of overseeing the progress of a biomedical study and ensuring that it is conducted, the data are collected and the study results are reported in accordance with the protocol, plan, programme, standard operating procedures and Good Clinical Practice.
- v. **Good Clinical Practice (GCP)** - a standard for the design, organization, conduct, monitoring, auditing and recording of clinical trials, as well as for the analysis and reporting of their results, that provides assurance that the data obtained and the results reported are credible and accurate, and that the rights, health and confidentiality of study subjects are protected.
- w. **Adverse incident** – any malfunction and/or deterioration in the characteristics or performance of a medical device, or any inadequacy or inaccuracy in the accompanying information (documentation) for a medical device, or side effects or an adverse reaction not specified in the instructions for use or the operating manual, which directly or indirectly led, or might have led, to the death or serious deterioration in the state of health of users or third parties.
- x. **Adverse event** – any untoward change in the state of health of a patient or clinical trial (study) subject administered a medicinal (investigational) product, regardless of whether it has a causal relationship with its use.
- y. **Impartial witness** - an individual not involved in the conduct of the clinical trial, - who assists the study subject, including by reading out the written materials supplied to him or her.
- z. **Non-interventional clinical trial** – a study that is conducted after the state registration of a medicinal product or medical device and is prescribed within the framework of medical practice.
- aa. **Original medical records** – see the term "source documents".
- bb. **Essential documents** – documents which collectively or individually permit evaluation of the conduct of a study and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice (GCP) and with regulatory requirements.
- cc. **Clinical trial (study) report** - a document containing a description of a clinical trial of a therapeutic, prophylactic or diagnostic agent involving a human as a subject, which integrates the clinical and statistical descriptions, the presentation of data and their analysis; and long-term effects, including adverse reactions to the investigational medicinal product or medical device.
- dd. **Source documents** – all information contained in original medical records and certified copies thereof that describes the results of clinical observations, examinations and other activities and makes it possible to reconstruct and evaluate the course of the clinical trial. Source data are contained in source documents (originals or certified copies thereof).
- ee. **Comparator product** – an authorised medicinal product or placebo used as a control in a clinical trial.
- ff. **Clinical trial protocol** - a document that describes the objectives, design, methodology, statistical considerations and organization of a study.
- gg. **Serious adverse event and/or serious adverse reaction** - an adverse reaction that results in death, is life-threatening, requires hospitalization of the patient or prolongation of existing hospitalization, results in persistent or significant incapacity or disability, or in congenital anomalies or birth defects, or requires medical intervention to prevent the development of the listed conditions

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- hh **Protocol synopsis** - a brief summary of the clinical trial protocol.
- ii. **Clinical trial sponsor** – an individual or legal entity responsible for the initiation, organization and financing of a clinical trial.
- jj. **Standard operating procedures** – detailed written instructions designed to achieve uniformity in the performance of a specific activity.
- kk. **Study subject** - an individual who participates in a clinical trial either as part of the group receiving the investigational product or as part of the control group.
- ll. **Authorized body** in the field of healthcare – the Ministry of Health of the Republic of Kazakhstan.

mm **Clinical trial phase:**

the first phase of a clinical trial – the first testing of a medicinal product, conducted in healthy volunteers or, where the high toxicity of the investigational product makes it unethical to conduct the study in healthy volunteers, in patients suffering from the relevant disease, in order to establish tolerability, safety, the presence of a therapeutic effect, and pharmacokinetic and pharmacodynamic characteristics;

the second phase of a clinical trial – a study aimed at assessing the efficacy and short-term safety of the investigational medicinal product in patients with a specific disease, as well as demonstrating the clinical efficacy of the medicinal product and determining the therapeutic dose level when tested in a group of patients;

phase four of a clinical trial – a study of a medicinal product conducted after its registration and placing on the market in order to confirm its therapeutic efficacy and the strategy for its further use, as well as to obtain additional information on the range and frequency of adverse effects and on the interaction of the investigational medicinal product with other medicinal products;

phase three of a clinical trial – a study conducted in large groups of patients of various ages and with various concomitant conditions in order to examine all aspects of treatment, including assessment of the risk: benefit ratio.

No. Abbreviations

- a. **IB** – Investigator's Brochure
- b. **PI** – Principal Investigator
- c. **RT** – research team
- d. **MD** – medical device
- e. **IP** – investigational product
- f. **CRF** – case report form
- g. **IC** – informed consent
- h. **CT** – clinical trial
- i. **CTC** – clinical trial coordinator
- j. **LEC** – Local Bioethics Committee of HemCenter LLP
- k. **MoH RK** – Ministry of Health of the Republic of Kazakhstan
- l. **AE** – adverse event
- m. **ED** – essential documents
- n. **RK** – Republic of Kazakhstan
- o. **SAR** – serious adverse reaction
- p. **SAE** – serious adverse event
- q. **SOP** – standard operating procedure
- r. **LLP** – limited liability partnership
- s. **the Center** – HemCenter LLP
- t. **CBC** – Central Bioethics Commission of the Ministry of Health of the Republic of Kazakhstan

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- u. **ҚР ДСМ** – abbreviation used when assigning numbers to regulatory legal acts of the RK (Kazakh)
- v. **CRO** – contract research organization
- w. **GCP** – Good Clinical Practice
- x. **ICH-GCP** – International Conference on Harmonisation, the international conference on the harmonisation of GCP
- y. **CIOMS** – Council for International Organizations of Medical Sciences
- z. **EMA** – European Medicines Agency (EMA), the agency for the evaluation of medicinal products for compliance with the requirements set out in the European Pharmacopoeia
- aa. **FDA** – Food and Drug Administration of the USA (United States of America)
- bb. **UNESCO** – United Nations Educational, Scientific and Cultural Organization, a specialised agency of the United Nations for education, science and culture.
- cc. **WHO** – World Health Organization

No. Procedure

1. **Procedure for receiving the submitted documents** On receipt of the study document package, the LEC Secretary carries out a preliminary check of them.
The LEC Secretary must sign and date, certifying receipt of the documents, in accordance with the established form (see the Standard Operating Procedure "Submission of an application for review of a study document package") and returns a receipt in the established format to the person who delivered the document.
2. **Procedure for checking the completeness of the content of the documents** The LEC Secretary compiles a special package containing the study documents and distributes the packages for review to the LEC members or to the independent consultants engaged in the review.
The LEC member or the independent consultant engaged in the review of the study documents checks the submitted document package:
for full compliance of the documents with the assessment form;
determines the time frame for conducting the review;
checks the date of the next LEC meeting and whether the applicant can attend it If any materials/ documents required for the assessment are found to be missing, the LEC members or the independent consultant must inform the LEC Secretary.
3. **Review of the study document package**
 - 3.1 **Initial review of the application**
The LEC member or independent consultant conducts the initial review of the document package
 - 1) the application check the application form (see the Standard Operating Procedure "Submission of an application for review of a study document package") for completeness of the information provided/ of its completion and for the presence of the signatures of the Principal Investigator/ study lead and of the LEC Chair and Secretary.
check the initial application review form and attach it to the study protocol (Appendix 1)
When reviewing the study protocol, the assessment is carried out in accordance with the requirements applicable to the type of study (Appendix 2).
 - 3.2 **Assessment form**
The LEC member or independent consultant conducts the initial review of the document package using the established assessment form (Standard Operating Procedure "Assessment of study documentation"). The completed assessment form is the official record of the decision taken by the LEC in respect of the particular study document package.
When carrying out the review assessment, the LEC member or independent consultant must pay attention to the following criteria:
minimisation of risk to study participants;

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the risk to participants must be justified in relation to the expected benefit; the selection of participants is equitable and impartial;

the informed consent must be clear, understandable and properly documented; the study plan makes adequate provision for monitoring the data collected in order to ensure the safety of participants;

there are adequate provisions to protect privacy and to maintain confidentiality where necessary;

appropriate measures are in place to protect vulnerable participants;

recording of comments where necessary;

signature of the reviewer and date

4. **Presentation of the review results at a meeting of the Local Bioethics**

Committee of HemCenter LLP

The primary reviewer presents a brief summary (orally or in writing) of the document package/ study protocol together with his or her comments.

The LEC Chair or Deputy Chair initiates a discussion of all the documents under consideration (study protocol, Investigator's Brochure, informed consent, qualifications of the investigator and of the study site, advertising materials).

Recommendations for changes to the protocol, the informed consent form and/or the advertising materials are recorded in the meeting minutes as "amendments proposed by the LEC" and sent to the investigator.

The LEC Chair or Deputy Chair calls a separate vote on each item. The LEC members vote, recommending one of the following options:

to approve the conduct of the study without comments;

to approve with LEC recommendations, i.e. after the comments have been addressed, without re-review, provided that the questions raised are answered and the recommended changes and/or additions are made as a routine matter. In this case the amended documents and/or supplemented documents must be approved by the LEC Chair or Deputy Chair.

to approve subject to resubmission of the documents, i.e. to re-review at an LEC meeting after changes have been made to the study procedures and materials. In doing so, the LEC clearly formulates all the questions and objections that have arisen.

to reject - not to permit the conduct of the study (stating the reasons for refusal). **In the case of a favourable decision (without comments)**

If a favourable decision is issued on the document package/ study protocol, the LEC specifies how frequently the ongoing review of the study will be conducted.

The Secretary sends the applicant/investigator a decision letter together with the approved documents. The letter must contain a list of all the documents approved by the LEC and state the time frames for the ongoing review and for verification of the investigator's fulfilment of other obligations throughout the study. The date of LEC approval is indicated on every page of the approved informed consent form.

In the case of an unfavourable decision (rejection)

If the LEC votes to reject the application, the LEC Secretary immediately informs the applicant in writing of the decision taken and of the reasons for rejecting the application.

If the investigator decides to appeal, this can be done by contacting the LEC Secretary. The appeal procedure must be described in the LEC decision letter sent to the applicant.

In the case of a decision that changes are required

If the LEC has voted for changes to be made to any of the documents, the LEC Secretary either makes the required changes or sends the applicant a written notice requesting that the amendments be made and the documents resubmitted to the LEC.

5. **Preliminary notification of the decision** The LEC Chair sends the electronic version of the completed assessment form to the LEC Secretariat within one day, but no later than 5 working days after the decision is

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taken. The LEC Secretary in turn forwards the LEC decision to the lead/ Principal Investigator (by e-mail) and documents the incoming and outgoing correspondence in the protocol file.

6 Final notification of the decision

5.1 Signing of the approval

After the decision has been taken, the relevant forms must be obtained and completed, and the LEC Chair then signs and dates them.

5.2 Assessment form

The LEC member or independent consultant completes the assessment form, which is then signed by the LEC Chair.

5.3 Application form for review

The applicant must obtain the signature of the LEC Chair, date the original form within 5 (five) working days and return it to the LEC Secretary. The assigned number is to be entered in the boxes at the bottom of the form, filled in sequentially – the first three boxes show the serial number of the decision, after the next stroke – the current month, and after the hyphen – the current year. The LEC Secretary signs and dates the form.

An extract from the minutes of the meeting held, containing the LEC decision on the submitted project, is issued to the applicant no later than 10 working days after the meeting (Appendix 3).

The LEC Secretary is responsible for notifying applicants and bringing the results of the consideration of projects to their attention, which he or she records in the relevant log.

5.4 Action letter

An action letter must be prepared to inform the investigator or the head of the research project of the LEC decision. In doing so, it is necessary to:

state clearly the actions that the investigator must take

in the case of an unfavourable decision, the notice to the investigator or project head must contain the following: if you wish to appeal against this decision, inform the LEC and submit a written appeal, with the grounds for it, addressed to the LEC Chair

check the accuracy of the wording and the spelling of the letter send the letter to the applicant within 7 working days

7 Storage of documents

A copy of the letter must be kept in the correspondence file. The originals of the documents (applications for review and the assessment form) are to be placed, in accordance with their serial number, in the "Decisions Taken" folder. The file must be kept on the appropriate shelf in the room designated for this purpose

Appendix 1

Application form for initial review

Contact details of the study site: _____

Title

Address: _____

Telephone: _____

Fax: _____

E-mail address: _____

Appendix 2

Outline of the study protocol (ethical review)

I. Title page

1. Title (topic) of the study, identification number, date. Any additions (changes) must also be numbered and dated.

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2. Surname of the study lead (or sponsor).
3. Surname, position and academic title of the investigator; name and address of the organisation where the study is conducted.
- II. **Purpose of the study and introduction.**
 1. Purpose of the study. State the scientific aims and objectives of the study.
 2. Introduction. Describe here the rationale for the purpose and the references.
- III. **Criteria for the selection of study participants.**
 1. Number of participants. State the total number of participants planned for this study. In the case of a multicentre study, state the total number of participants for the study as a whole
 2. Distribution by sex. Describe the anticipated gender distribution. If there is any restriction on inclusion in the study by sex, explain the nature of this restriction and the rationale. Equal inclusion of both men and women in the study is important for the equitable sharing of the benefits and burdens of the research. Therefore, participants of both sexes must be included in the study unless there are other relevant medical and scientific reasons.
 3. Age. State the age range of the participants. Provide the rationale for the choice of these age limits. The participation of adults in the study must not be restricted by age unless there are other medical or scientific reasons.
 4. Nationality (ethnicity). Describe the anticipated racial and ethnic distribution of the participants. If there is any restriction by national/ethnic origin, explain the nature of the restriction and provide the rationale. The study must include a sufficient number of people of different national and ethnic origin living in the region concerned to ensure that the benefits and burdens of the research are equitably distributed.
 5. Inclusion criteria. List the criteria for inclusion in the study. These criteria must be scientifically justified and define who may be included in the study.
 6. Exclusion criteria. List the exclusion criteria. They must be scientifically justified and help to define the participant population more precisely.
 7. Vulnerable groups. If vulnerable participants (with limited capacity for independent decision-making) are to be included in the study, there must be a justification for this. Children, pregnant women, the elderly, students, subordinate employees, embryos and prisoners are considered vulnerable participants who require greater protection.
- IV. **Methods and procedures**
 1. Methods and procedures. Briefly describe the study design and all procedures that will be used to achieve the objectives of the project. Procedures/tests/interventions that are experimental and/or used solely for the study must be identified and distinguished from those that will be applied regardless of the study (i.e. for the provision of medical care). Highlight any procedures, situations or materials that may cause harm and call for precautionary measures. Identify routine procedures that will be performed for scientific purposes only (additional tests).
 2. Data analysis and monitoring. Briefly describe the statistical/analytical methods to be used. For trials involving interventions that may pose a potential risk, a data monitoring committee/commission may be required to protect the safety and well-being of participants. Provide a detailed description of its governance (membership, functioning, frequency of review, stopping rules, etc.).
 3. Data storage and confidentiality. Describe where the data obtained will be stored during the study and how they will be protected. The investigator must take the necessary steps to ensure the confidentiality of the data. This includes coding the data and selecting an appropriate data storage mechanism that will prevent unrestricted access to the data. Indicate who will have access to the data and how they will be used.
- V. **Risk/benefit assessment**
 1. Level of risk. Indicate the level of risk posed by the study according to the following categories: minimal, greater than minimal. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the study are not greater than those ordinarily encountered in daily life or during routine

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physical or psychological tests. Risk is the potential damage associated with the study that a reasonable person would regard as harmful to health.

2. Potential risk. Describe the potential risk associated with the study. Risks are not only physical but also psychological, sociological, economic and legal. This includes any specific toxicity data noted in the Investigator's Brochure. If possible, estimate the probability of such damage occurring and indicate its potential reversibility.
3. Protection against risk. Describe how the study design will protect against and/or minimise potential risk or discomfort. Potential risk or discomfort must be minimised as far as possible through the use of such procedures as staff training, monitoring, withdrawal of a participant upon evidence of adverse reactions or side effects; indications for treatment, counselling and other necessary follow-up steps. Indicate who will pay for this.
4. Potential benefit to the participant. Describe the potential benefit, if any, to the study participants. If no benefit is expected, state this.

Payment for participation is not considered a benefit.

5. Alternatives for the participant. This section must include a description of the alternatives available to a participant who has chosen not to take part in the study. If the participants are students who will receive academic credits for participation, describe alternative ways of obtaining equivalent credits.
- VI. **Identification of study participants, recruitment and consent.** If recruitment and prior consent are not applicable, as in the case of emergency and urgent medical care studies or studies of already existing data/materials, you may answer only the first question on the identification of the study population and explain why recruitment and consent are not applicable in this study.
 1. Methods of identifying and recruiting participants. Describe the methods that will be used to identify and recruit prospective participants. These methods must ensure confidentiality and be free from coercion. Recruitment of the investigator's students, subordinates and patients is regarded as potentially coercive, and steps must be taken to minimise coercion.
 2. Consent process. Describe who will obtain consent and how the informed consent process will be structured so as to facilitate rational and thoughtful decision-making by the participant/his or her legal representative without any element of coercion or duress. Only the persons listed in this section are entitled to obtain consent.
 3. Participant's condition. If not all participants will be able to give informed consent, describe how their condition will be assessed. Describe the expected degree of impairment affecting their capacity to consent to participate in the study. Studies involving persons with limited capacity are permitted only for studies with minimal risk or direct benefit.
 4. Comprehension. All investigators have a legal and ethical obligation to ensure that prospective subjects or their representatives have sufficient knowledge and understanding of the elements of informed consent to enable them to make an informed and considered decision whether or not to participate, or to permit participation in the study. In this section, describe how it will be determined that the subject or his or her legal representative has understood the information provided. This section must clearly set out an adequate plan to ascertain an acceptable level of comprehension before consent is obtained. If children and/or legally incapacitated adults will participate, this section must also include a specific plan for assessing comprehension at the time consent is obtained.
 5. Consent forms. Review the EC's recommendations on the informed consent (IC) form and on those IC items that are required to be documented. The title page of the IC must be printed on the letterhead of the department or institute.
 6. Documentation of consent. The responsible investigator is responsible for obtaining and documenting IC from all subjects. Describe the process of documenting and storing IC, if this has not already been done in other sections.
 7. Cost of participation. Describe and justify the cost of participation to the subject. This section must clearly define who will pay for study-related procedures. As a rule, subjects should not pay for research

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procedures that are of no direct benefit. There must be no charge to participants where the project is funded by a grant, contract or other means of financing.

8. Payment for participation. Describe the reimbursement or payment that subjects will receive for participation. List the conditions that subjects must fulfil in order to receive payment or remuneration. The amount must be justified and must not coerce the subject into participating. A participant need not take part until the end of the study in order to receive payment. This is necessary to protect his or her right to withdraw from the study without penalty.

Appendix 3

Extract/ written decision

Application number and date	LEC decision
Meeting No.	Date (DD/MM/YY)

Study title

Lead investigator: _____

Study site:

Items reviewed:	☐ attached ☐ not attached
Re-review	Date of previous review

☐ yes

☐ no

Decision:	☐ Approved ☐ Approved with recommendations ☐ Resubmission ☐ Not approved
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Protocol No. _____ Assigned number _____ LEC Chair LEC Secretary

Date: «__» _____

Governing documents

1. Code of the Republic of Kazakhstan "On Public Health and the Healthcare System" No. 360-VI ZRK dated 7 July 2020. [Link](#)
2. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 248/2020 dated 11 December 2020 "On approval of the rules for conducting clinical trials of medicinal products and medical devices, clinical laboratory testing of medical devices for diagnostics outside a living organism (in vitro), and the requirements for clinical sites, and for the provision of the public service Issuance of authorisation to conduct a clinical trial and (or) testing of pharmacological and medicinal products and medical devices". [Link](#)
3. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 35 dated 4 April 2022, registered with the Ministry of Justice of the Republic of Kazakhstan on 12 April 2022 under No. 27526, on amendments and additions to Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 248/2020 dated 11 December 2020 "On approval of the rules for conducting clinical trials of medicinal products and medical devices, clinical laboratory testing of medical devices for diagnostics outside a living organism (in vitro), and the requirements for clinical sites, and for the provision of the public service Issuance of authorisation to conduct a clinical trial and (or) testing of pharmacological and medicinal products and medical devices". [Link](#)
4. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 310/2020 dated 21 December 2020 "On approval of the rules for conducting biomedical research and the requirements for research centres". [Link](#)
5. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 181/2020 dated 4 November 2020 "On approval of the rules for assessing, within the framework of pharmaceutical inspection, the

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materials of preclinical (non-clinical) studies and the compliance of the conditions for conducting them with the requirements of Good Laboratory Practice (GLP) of the Republic of Kazakhstan and (or) the Eurasian Economic Union". [Link](#)

6. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 151/2020 dated 23 October 2020 "On approval of the Regulation on the Central Bioethics Commission". [Link](#)
7. Order of the Acting Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 130 dated 20 December 2021 "On approval of the standard for the organisation of haematological care for the adult population of the Republic of Kazakhstan". [Link](#)
8. Order of the Acting Minister of Health of the Republic of Kazakhstan dated 4 February 2021 No. ҚР ДСМ-
15. Registered with the Ministry of Justice of the Republic of Kazakhstan on 9 February 2021 under No. 2216, "On approval of good pharmaceutical practices". [Link](#)
9. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 304/2020 dated 21 December 2020. Registered with the Ministry of Justice of the Republic of Kazakhstan on 22 December 2020 under No. 21848, "On approval of the regulations on the clinical site, the clinic of a healthcare education organisation, the university hospital, the residency site and the integrated academic medical centre, and the requirements for them". [Link](#)
10. Order of the Minister of Health of the Republic of Kazakhstan No. ҚР ДСМ- 299/2020 dated 21 December 2020 "On approval of the rules for accreditation in the field of healthcare". [Link](#)
11. Standard ISO14155:2014№ "Clinical investigations. Good Clinical Practice". [Link](#)
12. Recommendation of the Board of the Eurasian Economic Commission No. 11 dated 17 July 2018 "On the Guideline on general issues of clinical trials". [Link](#)
13. Decision of the Council of the Eurasian Economic Commission No. 79 dated 3 November 2016 "On approval of the Rules of Good Clinical Practice of the Eurasian Economic Union". [Link](#)
14. Recommendation of the Board of the Eurasian Economic Commission No. 19 dated 3 November 2020 "On the Guideline on the application of biostatistics principles in clinical trials of medicinal products". [Link](#)
15. Recommendation of the Board of the Eurasian Economic Commission No. 18 dated 27 October 2020 "On the Guideline on safety pharmacology studies of medicinal products for human use".
16. Decision of the Council of the Eurasian Economic Commission No. 85 dated 3 November 2016 "On approval of the Rules for conducting bioequivalence studies of medicinal products within the Eurasian Economic Union". [Link](#)
17. Declaration of Helsinki of the World Medical Association, June 1964 (latest revision of 9 July 2018). [Link](#)
18. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, World Health Organization (2011); and other international declarations and guidelines in the field of research ethics (WHO, ICH-GCP, UNESCO, CIOMS, CE).
19. Regulation on the Local Bioethics Committee (hereinafter- the LEC or the Committee) of HemCenter LLP, approved by Order No. I-02-44 dated 31 June 2023
20. Rules for conducting clinical trials and scientific research at HemCenter LLP, approved by Order No. I-02-47 dated 31 June 2023
21. Job descriptions of the Local Bioethics Committee of HemCenter LLP dated 31 June 2023.
22. Other regulatory legal acts of the Republic of Kazakhstan governing clinical trials.

Related documents

No.	type	title
Issl-3-1	SOP	Maintaining Confidentiality in the Work of the LEC
Issl-3-4	SOP	Process of Submitting an Application for Review of the Study Document Package (Study Protocol, etc.)

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Title	INITIAL REVIEW OF RESEARCH DOCUMENTATION (APPLICATIONS, STUDY PROTOCOLS)						
Issl-3-5		SOP			Assessment of a Study Application		

List of changes

Rev. No. Date	Order No. List of changes Change of the SOP form, corrections to terminology based on amendments/additions to the regulatory legal acts of the RK, corrections throughout the text
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Document acknowledgement list

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