**FORM A-4**

**Registration number \_\_\_\_\_\_\_\_\_\_**

**Date of application\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**RESEARCH PROTOCOL**

1. Title of research:

2. Introduction with an extended review of the literature on the topic

3. Study type - a complete description of the study design

4. The purpose of the research work

5. Objectives of research work

6. Planned start and duration of the study

7. Scientific novelty

8. Theoretical and practical significance

9. Substantiation of the choice of the experimental model. Substantiation of the impossibility of conducting research without the participation of animals. The choice of the object of research (species, sex, age, number of animals) with a description of the conditions of keeping, feeding, carrying out painful procedures, methods of anesthesia and euthanasia, the method of sampling.

10. Type of biomaterial (pathological or forensic autopsy, biopsy, operational (including archival), objects, quantity, methods of withdrawal;

11. Research methods, including methods of statistical analysis.

12. Expected results

**CRITERIA FOR THE SELECTION OF STUDY PARTICIPANTS IN THE CASE OF THE PARTICIPATION OF HUMANS.**

1. **Number of participants.** Indicate the total number of participants planned for this study. In the case of a multicenter study, indicate the total number of participants for the entire study as a whole. Give the formula for calculating the sample.
2. **Distribution by gender.** Describe the estimated gender distribution. If there is any gender restriction for inclusion in the study, explain the nature of the restriction and the rationale. Equal inclusion of both men and women in research is important to equally share the benefits and burdens of research. Therefore, participants of both sexes should be included in the study unless there are other relevant medical and scientific reasons.
3. **Age.** Please indicate the age range of the participants. Provide a rationale for choosing these age limits. Adult participation in a study should not be age-restricted unless there are other medical or scientific reasons.
4. **Nationality (ethnicity).** Describe the expected racial and ethnic distribution of the participants. If there is any restriction by nationality / ethnicity, explain the nature of the restriction and provide justification. Research should include a sufficient number of people of different nationalities and ethnicities in the region to ensure that the benefits and burdens of research are evenly distributed. If you want to take into account the ethnicity of the participants, then describe in detail how the group will be formed
5. **Criteria for inclusion.** List the criteria for inclusion in the study. These criteria must be scientifically based and determine who can be included in the research.
6. **Criteria for exclusion.** List the criteria for exclusion. They should be scientifically sound and help to more accurately determine the population of participants.
7. **Vulnerable groups.** If vulnerable participants (with disabilities for independent decision making) will be included in the study, there must be a justification for this. Children, pregnant women, the elderly, students, subordinate workers, embryos, military personnel and employees of law enforcement and special state bodies, persons held in institutions of the penitentiary system,are considered vulnerable participants who need more protection.
8. **Methods and procedures** Describe in detail the research plan by year, the time frame, and all the procedures that will be used to achieve the project goals. The multiplicity of invasions and interventions. The volume of biomaterial sampling with justification. Procedures/tests/interventions that are experimental and / or used exclusively for the study should be defined, described, and separated from those that will be used independently of the study (i.e., those that are included in the diagnostic and treatment protocol). Highlight any procedures, situations, or materials that may cause harm and involve the use of precautionary measures. Identify routine procedures that will only be performed for scientific purposes (additional tests). Describe in detail the research methods, the reagents used, the test systems with the full name of the country of manufacture and the equipment used with a valid verification certificate. If the transport of the material is provided (in the laboratory of the city and abroad), describe in detail the procedure for storing and transporting the material to the laboratory. Attach to the research protocol all the questionnaires, questionnaires, scales, algorithms, and individual registration cards used in the work. Scales or algorithms (diagnostic or other) used in the original language do not require validation and permission of the author (in cases for individual use by the researcher), if they are recognized and used in world practice (in the current part, specify the corresponding publication with links). If the researcher plans to implement these procedures after completing the research, it is recommended to translate them into Russian and state languages (attach the original). After the translation into Russian with the reverse translation into the original language in the pilot project, conduct research and publish, for translations into Kazakh, additionally pass the approval procedure in the Termincom committee with the provision of relevant documents.

*When submitting an application, specify the summary data, and the work carried out on validation and/or translations, by the members of the LBC will be monitored in interim reports.*

1. **Data analysis and monitoring.** Briefly describe the statistical / analytical methods used. For trials using interventions that may pose a potential risk, a data monitoring committee / panel may be required to protect the safety and well-being of participants. Give a detailed description of its governance (membership, functioning, frequency of examination, termination rules, etc.).
2. **Data storage and confidentiality.** Describe where the acquired data will be stored during the study and how it will be protected. The researcher must take the necessary steps to ensure the confidentiality of the data. This includes encoding the data and choosing an appropriate storage engine that will prevent free access to the data. Specify who will have access to the data and how it will be used.

**Assessment of the risk/benefit ratio.**

1. **Degree of risk.** Indicate the degree of risk that the study poses in the following categories: minimal, more than minimal. Minimal risk means that the likelihood and magnitude of harm or discomfort expected in the study is no greater than what is usually found in everyday life or during routine physical or psychological tests. Risk is the potential harm associated with research that would be considered harmful to health by a sane person.
2. **Potential risk.** Describe the potential risk associated with the study. The 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, assess the likelihood of this damage occurring and indicate the potential reversibility.
3. **Protection against risk.** Describe how the research design will protect and / or minimize potential risk or discomfort. Potential risk or discomfort should be minimized as much as possible through the use of procedures such as staff training, monitoring, exclusion of the participant after evidence of adverse reactions or side effects is obtained; indications for treatment, counseling and other necessary follow-up steps. Indicate who will pay for this.
4. **Potential benefits for the participant.** Describe the potential benefit, if any, for the study participants. If there is no expected benefit, indicate it. Participation fees are not considered a benefit.
5. **Alternatives for the participant.** This section should include a description of the alternatives that are provided for the participant who chose not to participate in the study.
6. **Study participant’s identification, recruitment and consent.** If recruitment and prior consent are not applicable in the case of studies in emergency and emergency care settings or in the case of reviewing existing data / materials, you can only answer the first question about the definition of the study population and explain why recruitment and consent are not applicable in this study.
7. **Methods for identifying participants and their recruitment.** Describe the methods that will be used to identify and recruit prospective participants. These methods must ensure confidentiality and be free from coercion. The recruitment of researcher students, subordinates, and patients is considered potentially coercive and steps should be taken to minimize coercion.
8. **Process for obtaining consent.** Describe who will obtain consent and how the informed consent process will be structured to facilitate rational and thoughtful decision-making by the participant / legal representative without any elements of coercion or violence. Only those people who are listed in this section are eligible to obtain consent.
9. **The state of the participant.** If not all participants will be able to give informed consent, describe how their condition will be assessed. Describe the expected degree of damage associated with their ability to consent to participate in the research. Research with people with disabilities is only allowed for research with minimal risk or direct benefit.
10. **Understanding.** All researchers have a legal and ethical responsibility 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 informed decision to participate or not; or allow participation in the study. In this section, describe how it will be determined that the subject or his legal representative understood the information provided.

This section should clearly reflect an adequate plan to ensure an acceptable level of understanding before consent is obtained. If children and / or disabled adults will participate, this section should also include a specific plan for assessing understanding at the time of consent.

1. **Forms of consent.** Explore the recommendations of the LEK on the form of informed consent (IS) and those IS clauses that are required for documentation. The IP title page should be printed on the letterhead of the department or institute.
2. **Documenting consent.** The responsible executor is responsible for obtaining and documenting IP from all entities. Describe the process for documenting and storing IP, if not already done in other sections.
3. **Participation price.** Describe and justify the cost of participation for the subject. This section should clearly define who will pay for the research procedures. Usually, subjects should not have to pay for research procedures that do not directly benefit them. There should be no fees from the participants in the case of a grant, contract or other means of financing the project.
4. **Participation fee.** Describe the refund or payment that the subjects will receive for participating. List the conditions that must be met by the test subjects in order to receive payment or remuneration.

**Note:** If you plan to involve third-party organizations in cooperation in the study or request confidential information, you must attach a cooperation agreement or permission to access their databases, or indicate that you plan to obtain such documents.

**IN THE CASE OF research ON LABORATORY ANIMALS**

1. Types of research:

• The nature of the research (acute or chronic experiment);

• Detailed description of the chosen research model;

2. Description of animals and conditions of keeping: species, line, sex, age, weight, source of production, method of marking them, information on their care, environment, feed ration and source of production.

3. Reproduction (if provided). Indicate the further fate of the offspring, its participation in experiments.

4. Detailed and step-by-step description of the impact on the animal. Methods used during the experiment:

a) at the preparatory stage:

- introduction of chemicals, food additives, physical and mechanical effects.

b) at the main stage:

- the method of sampling the experimental material, a list of the material to be taken, whether the killing of the animal is envisaged, if so, in what way.

- it is necessary to provide a description of the anesthesia performed, the type of drugs used.

c) at the final stage (use of the animal after the experiment, description of the method of utilization of animal biological material).

1. Description of the used biochemical, immunological, histological, histochemical, cellular-molecular, physiological, morphological and other methods of research and processing of the information received;

6. Have similar studies been conducted (or are being conducted) before? If so – with what result?

7. Data analysis;

8. Applications.

Principal Researcher \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_(Signature)

"\_\_\_" \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_20\_.