

The Development of Institutional Program for the Laboratory Animals Housing and Use

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ABSTRACT

This study aims to investigate the research work results, which prove the possibility of using biographical analysis techniques to develop prospective teachers to measure the mental states of the students. The biographical strategy and procedures for the examination of mental states are examined at the interdisciplinary level. It has been revealed that biography describes a philosophy of this phenomenon through life's retrospective prism and as a response that shows an individual's outlook on their mental features in numerous social circumstances. To interpret that, a pedagogical and psychological study is conducted—this study had no analog theory and use of subjective and pedagogical science. The mentioned study has been conducted in 4 levels: organizational stage—this stage is completed to demonstrate the technical and methodological interpretation of experimental work; ascertaining step—the predictive implies to discover the willingness levels of prospective teachers to employ the methods of biographical analysis in examining the students' mental states have been investigated; formative step—it indicates the author's methodology for promoting the prospective teachers' knowledge, skills, talents to use biographical methods in analyzing the students' mental states as well as their correction; control step—this stage illustrates the outcomes of psychological and pedagogical experiment. Based on the results acquired, it can be inferred that the author's teaching approaches' effectiveness is to apply biographical methods to develop prospective teachers to measure and resolve students' mental states. Furthermore, this matter helps manifest that biographical strategies and the fundamental psychological are excellent in diagnosing personality.

Key words: Institutional program for the laboratory animals use, IACUC, Animal research protocol, Ethical examination, Three rs standards, Experimental animal work.

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INTRODUCTION

Society is currently concerned about the ethical aspects of the animals use in research procedures.

Current trends require animals to be treated as sentient beings, and their use in scientific and practical procedures should be limited to those areas that ultimately benefit human, animal and environmental health.

The care of animals and their use in scientific experiments is regulated according to the generally recognized international principles

of Replacement, Reduction and Refinement [1,2], which should be in accordance with national standards. It is important to consider the "three Rs" principles in the following hierarchy: starting with the requirement to use alternative methods instead of experiments with animals - Replacement, then reducing the number of animals used by choosing optimal experimental ways-Reduction and applying methods to improve the quality of their use - Refinement.

The principles of humane treatment and rational use of laboratory animals emphasize the importance of research on animals for human health, the development of science and the welfare of the community and include such scientific and methodological approaches as:

- ✓ The use of proper animal species of reasonable quality in minimum enough.
- ✓ Elimination or minimization of discomfort, pain and distress and the use of sedatives, analgesics and anesthetics.
- ✓ Determination of the experiment end points.
- ✓ Provision of qualified animal care and carrying out the experimental procedures on live animals by the experienced staff.

In the institution where research with laboratory animals is carried out, the institutional program for the laboratory animals housing and use is being developed, which describes in detail the actual housing conditions of the laboratory animals, the amount of veterinary aid, the staff qualifications and training, biosafety issues in the experimental vivarium, vivarium infrastructure and equipment, as well as regulations for the functioning of the local ethical commission to control all aspects of the animals housing and use in the institution [3,4].

The basis of institutional program for the laboratory animals housing and use is the policy of the institution with the approval and use of the principles of humane treatment of laboratory animals and their rational use in all areas of the organization. The policy contains the obligations of the institution to control the housing and use of animals, provide animals with adequate veterinary aid and requirements for the staff qualifications and training [4].

A well-formed and functioning Institutional Animal Care and Use Committee (IACUC) [5] is responsible for the implementation of the institutional program for the laboratory animals housing and use. The role of the IACUC committee is to organize the ethical review process for conducted research, monitor animal care, and provide training for vivarium staff and researchers.

The roadmap of institutional program for the laboratory animals housing and use is the Animal Research Protocol, which is a request sent to the IACUC to conduct a study with animals with a schematic description of the experiment, the species and number of animals, housing conditions, manipulations, painful procedures, methods of euthanasia, with a description of the risks, as well as written guarantees from the leading researcher [6]. The application protocol must justify the goal of the experiment with animals and show the absence of alternative methods.

In this work, we tried to assess the impact of the implementation of the institutional program for the laboratory animals housing and use on the planning of experimental work with laboratory animals by research workers / researchers.

MATERIALS AND METHODS

When creating institutional program for the laboratory animals housing and use in our organization, we were guided by the strategy for the development of such a program [3], and the policy of our organization, which declares the recognition and implementation of the "Three Rs" principles and the conduct of ethical review of all the procedures with laboratory animals.

The term "ethical review" refers to the definition, formulated by FELASA (Federation for Laboratory Animal Science Associations), to ensure an adequate and clearly formulated objectives for the use of animals at all stages of scientific work, from initial planning to obtaining the results and their analysis [7]. "Ethical review" includes consideration of the following issues:

- ✓ Study of the possibility of achieving the goal using alternative methods without the use of animals.

- ✓ Maintaining the balance between the expected benefits of the experiment and the harm caused to the animals.
- ✓ The probability of achieving the goals of the research at the given design of the experiment, the given conditions of housing animals and the qualifications of the employees.
- ✓ Minimizing animal suffering and improving their state, optimizing animal housing and care standards; effective staff training and management of all employees involved in the work.

In our institutional program for the laboratory animals housing and use, first of all, the Mission (policy) of the scientific center, general provisions and definitions are defined. The description of the vivarium complex is presented, including premises, engineering solutions, equipment, and the vivarium staff qualification. A separate chapter regulates the powers, functions of the IACUC committee, requirements for the composition of the IACUC and the organization of its activities. It also describes the organization of consideration of complaints and suggestions regarding non-compliance with requirements for ensuring animal welfare. An integral part of the program is the Animal Research Protocol.

The developed Animal Research Protocol is reviewed within no more than 14 days and at least by 2 experts and includes the following information:

- ✓ Section 1: Basic information about the application, including the data of the basic researchers, overview and line of research, biosafety requirements, and information on the source of funding.
- ✓ Section 2: Planning and methods of carrying out the experiments with laboratory animals, including experiment design, alternative methods substantiation and data, information on the species of animal, number, age, gender and weight, description of the

animals housing conditions, identification and veterinary supervision.

- ✓ Section 3: Animal treatment procedures, which indicate all planned animal manipulations (capture, fixing, injection, sample collection, behavioral testing, surgical procedures, anesthesia and euthanasia techniques, toxicity tests).
- ✓ Section 4: Pain classification and assessment, the degree of stress in the animal. Here it is necessary to describe the levels of pain and stress in animals by categories B, C, D and E, depending on the manipulation and methods of reducing the pain and stress of the animal.
- ✓ Section 5: An assurance by the researcher of the humane treatment of animals and their use in laboratory research with a personal signature.

Since 2020, we began to use an abbreviated application protocol, which, unlike the full one, did not have a section with a detailed description of the planned procedures and was considered by only one expert in an abbreviated time limits of 5 days.

9 people joined the IACUC committee, including a chairman, a secretary, a public representative and each 2 representatives from three organizations using laboratory animals, which ensured competent consideration of protocols with a wide range of subjects. Both the veterinary specialists and researchers with experience in experimental work on laboratory animals were present in the IACUC committee.

In total during 2019-2020 IACUC members reviewed 23 application protocols related to research goals, educational process and operational need (Table 1).

RESULTS AND DISCUSSION

From the 23 applications filed with the IACUC, 14 protocols had production purposes and amounted to 3280 laboratory animals (60.4%);

Table 1: Issue of laboratory animals in 2019-2020.

Seq No.	Animal species	Production purposes n (%)	Training n (%)	Scientific research n (%)	Total issued. n (%)
1	Laboratory mice (rodents)	2017 (37.1%)	503 (9.3%)	1643 (30.3%)	4163 (76.7%)
2	Laboratory rats	150 (2.8%)	-	-	150 (2.8%)
3	Guinea pigs (cavies)	1068 (19.7%)	-	-	1068 (19.7%)
4	Laboratory rabbits	45 (0.8%)	-	-	45 (0.8%)
Total n (%)		3280 (60.4%)	503 (9.3%)	1643 (30.3%)	5426

6 applications were for research purposes and amounted to 1643 animals (30.3%); 3 applications were for educational purposes and amounted to 503 laboratory mice (9.3%).

Basically, the researchers used laboratory mice - 4263 heads (78.6%), guinea pigs - 1068 (19.7%), rats - 150 (2.8%) and laboratory rabbits - 45 heads (0.8%).

Initially, for the review of protocols, IACUC used the full format of the application protocol, however, since the beginning of 2020, a abbreviated version of the application protocol has been developed for repetitive studies, to which all production protocols referred, and a procedure for their expedited review has been adopted. In addition to production work with animals, the abbreviated application protocol was also applied for cases related to an emergency when an expedited review of the application was required, and the IACUC chairman made a responsible decision on the approval of experimental work with animals. The correspondent provisions have been introduced into the institutional program for the laboratory animals housing and use.

Protocols for fundamental and applied scientific purposes and teaching were funded mainly by government science and technology programs and grants. These protocols underwent a full ethical review with peer review by two specialists. Production-oriented, privately funded animal research protocols have generally been reviewed under an expedited and abbreviated bioethical review protocol. All production protocols using experimental animals were justified in the form of legislative regulations and were always repeated in the same form. For example, tests for acute and chronic toxicity are regulated by the order of the Ministry of Health of the Republic of Kazakhstan No. 133 of 2008 [7], which clearly defines the use of experimental animals (mice, rats, guinea pigs and rabbits) and does not provide for the possibility of replacing methods with other alternative approaches.

When reviewing the research protocols, IACUC experts primarily paid attention to the following issues:

- ✓ Description of the qualifications and experience of the research team.
- ✓ Determining the species and number of

animals to be used, as well as the appropriacy of the species and numbers used.

- ✓ Substantiation for the use of animals, and information on alternative methods.
- ✓ A complete description of the intended use of the animals.
- ✓ A description of the procedures that may cause pain or anxiety to the animals, and what kind of pain relief or anesthesia will be used by the researchers.
- ✓ Description of the method of euthanasia used for humane killing at the end of the procedure or, if necessary, during the procedure.
- ✓ Compliance of the animals housing conditions with their species and whether they will contribute to their health and comfort.
- ✓ Provision of qualified veterinary services and trained staff for routine procedures.

In general, all 23 research protocols received approval, in which some of the scientific protocols received approval on the second and third attempts. All production protocols considered under the abbreviated protocol received approval from the first time.

As a result of the IACUC committee work and the consideration of the protocols, we faced a number of problems that differentiated them as organizational, training and tactical gaps in the institutional program for the laboratory animals housing and use.

Organizational gaps: failure to comply with the time limits for consideration of the application protocol, incorrect filling of the documentation by the researcher, contravention of procedure for drawing up and registering the application protocol and the process of its consideration.

Information and training gaps: insufficient training of IACUC members, researchers and vivarium staff, the absence of a training coordinator.

Tactical gaps: low efficiency of of production protocols research review, conflict of interests of the parties, commercial secrets, lack of ethical review effectiveness screening tool.

From the above gaps, the main problem faced by the IACUC committee is insufficient effectiveness of production protocols ethical review. Ensuring

the legitimacy of the research production protocols left no chances for the application of the 3R principles, since the current methodological documents regulated specific procedures with animals and were not subject to change. The effectiveness of the scientific protocols review based on the full Application Protocol was generally assessed quite high, as it corresponded to the goals of the institutional program for the laboratory animals housing and use and of the "three R" principles. However, IACUC experts are encouraged look at the ARRIVE guidelines (Abbreviations: Animal Research: Reporting of In Vivo Experiments) [8], which aims to improve the quality of reporting in animal research publications and can assist in the protocols review. The advantage of this document is that it adheres to the standards of the National Institutes of Health (NIH) [9] for the section "Materials, design, analysis and reporting" [10], and is a checklist of parameters for review - ARRIVE recommended set, therefore it focuses on the most important issues - the so-called critical minimum list. The minimum checklist includes information on research design, animal sample size, measures to reduce human bias, endpoints, statistical methods, experimental procedures, and results.

Gaps were found in the institutional program for the laboratory animals housing and use training for vivarium staff and researchers, showing low staff responsibility for experimental work and the inability of some IACUC members to effectively review protocols without proper training. Some researchers resisted the change, which also indicated the lack of information and training. Here, the important role of the training coordinator of the institutional program for the laboratory animals housing and use is noted, whose tasks include organizing and monitoring all types of trainings on working with animals for different types of staff, preparing training material and analyzing feedback.

There is an established practice in the world for the training and retraining of the staff working with laboratory animals. In particular, FELASA, which includes most of the European countries, has developed training programs for specialists at various levels. In the process of detailed development of these requirements, FELASA has pointed out four categories of persons relatable

to animal experiments (which are not mutually exclusive) [11,12]:

- ✓ Category A-Persons caring for animals.
- ✓ Category B-Persons carrying out experiments on animals.
- ✓ Category C-Persons responsible for the management of experiments on animals.
- ✓ Category D-Laboratory Animal Science Specialists.

Each curriculum includes a list of topics required to study and the content of training. For categories A and D, detailed vocational education is provided, while for categories B and C, relatively short courses are offered. The guiding principles of teaching are the principles of the "three Rs": methodological techniques improvement, a reduction of numbers of animals used and their replacement, where possible, with methods without involving creatures with consciousness and intelligence.

In category A, the degree of staff competence can be classified into four levels, where the achievement of each level together with relevant experience, where it is appropriate, may serve as a requirement for the transition to the next level:

- ✓ 1st level-Basic care for laboratory animals.
- ✓ 2nd level-1st level plus at least 2 years of practice.
- ✓ 3rd level-2nd level plus at least 3 years of practice.
- ✓ 4th level-Higher managerial position or specialty.

When considering the Application Protocols from three organizations, we faced the need to keep commercial secrets and ensure the purity of the review by preventing conflicts of interest. Since the Application Protocol contains the information sufficiently sensitive for the Customer, it is important for the Committee members to sign a document on confidentiality of information and non-disclosure. Corresponding provisions were also introduced into the IASILW program.

Registration of all incoming protocols is an important organizational approach [13] that allows to optimally select the experts, adhere to protocol consideration deadlines, which is

especially important for the principal researcher, contributes to the scientific discipline of the researcher and have a documented process for confirming IACUC expert activities for external audit.

Thus, in the process of introduction of the institutional program for the laboratory animals housing and use into the work of our organization, we have identified the following solutions for its improvement:

- ✓ The need to develop a program of various trainings, including the training for vivarium staff, for researchers and for committee members, especially for the training coordinator in accordance with the FELASA recommendations [14].
- ✓ Maintenance of confidentiality of some research protocols.
- ✓ Prevention of conflicts of interest, which may affect the ethical review effectiveness.
- ✓ Determination of ethical review effectiveness screening tool.
- ✓ Improvement of documented procedures with animals, considering the "three Rs" international standards.

CONCLUSION

The activities of organizations performing experimental work with animals should be carried out in accordance with the current national legislation and be based on the "three Rs" international standards. The high sanitary and hygienic requirements and serious moral and legal aspects of the staff work are imposed upon the institutions working with laboratory animals. The absence of national regulatory requirements harmonized with international analogues significantly reduces the process of proper examination of experimental work with animals, induces insufficient funding for the proper condition of the experimental vivariums premises, nurseries of laboratory animals, which can lead to adverse consequences for laboratory animals, for employees and the environment. For the evolution of ethical thinking, it is necessary to regulate at the state level the execution of ethical review before each use of experimental animals.

The introduction of the institutional program for the laboratory animals housing and use will

allow to direct the activities of the institution to comply with the principles of rational use of animals, to optimize work on labor protection and protection of employees, and to minimize the negative impact on the environment. Since the institutional program for the laboratory animals housing and use is highly human-driven, its important function is to train the researchers, vivarium staff and IACUC committee members.

It is important that the institutional program for the laboratory animals housing and use has the means of influence that guarantee the execution of decisions and give weight to the recommendations, which can only be provided by the administration of the institution.

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