Biomedical Journal of Indonesia
Journal Homepage: https://www.jurnalkedokteranunsri.id/index.php/BJI/index

Bioethical Principles of Use of Experimental Animals in Biomedical Research

Rachmat Hidayat[1*], Patricia Wulandari[2]

[1]Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Cattleya Mental Health Center, Palembang, Indonesia

ARTICLE INFO

Keywords:
Bioethics
Experimental Animals
Biomedical

***Corresponding author:**
Rachmat Hidayat

E-mail address:

dr.rachmat.hidayat@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/BJI.v7i1.13

ABSTRACT

Research is an activity carried out based on scientific principles and methods systematically to obtain information, data, and information from related subjects, with understanding the theory and proving assumptions and / or hypotheses. The results obtained are conclusions that can be applied or become additional knowledge for the advancement of science. However, research activities must still respect the rights and dignity of research subjects. Health research includes biomedical, epidemiological, social, and behavioral research. Some health research can be done in vitro, using mathematical models, or computer simulations.

1. Introduction

If the research results are to be used for humans, further research is needed using living materials (in vivo) such as cell lines and tissue cultures. However, to observe, study, and conclude all occurrences in living things as a whole, experimental animals are needed because experimental animals have a value for each part of the body and there are interactions between these body parts.[1,2] The experimental animal in the study is referred to as the semi-final test tube. Until now, health researchers are still conducting research using experimental animals, but there are still deficiencies in the handling and care of these experimental animals as regulated in the ethics of using experimental animals.[3,4]

This paper describes the general principles adopted in the use of experimental animals in research related to health, medicine, food and nutrition assessment. The research objective is to trigger the creation of a research protocol that can be accounted for both scientifically and ethically, including its application in the ethical submission form. The Need for Experimental Animals Test materials (drugs) intended for use in humans need to be investigated by including human subjects as the final test tube. Ethically human volunteers may be included if the material to be tested has passed the laboratory testing completely, followed by using experimental animals for its feasibility and safety. An experimental animal is any animal that is used in a biological and biomedical study which is selected based on the basic requirements or standards required in the research. In using experimental animals for research, sufficient knowledge is needed about various aspects of biological means, in terms of using laboratory

experimental animals. The management of experimental animals begins with the procurement of animals, including the selection and selection of types of animals suitable for the research material. [5,6] The management continues with the care and maintenance of animals during the study, data collection, until finally termination of the experimental animals in the study. Rustiawan A, describes several reasons why experimental animals are still needed in research, especially in the fields of health, food and nutrition, among others: (1) the diversity of research subjects can be minimized, (2) research variables are easier to control, (3) the life cycle is relatively short so that multigenerational research can be carried out, (4) the selection of animal species can be adjusted to the sensitivity of the animal to the research material being carried out. (5) relatively low cost, (6) can be carried out in high-risk research, (7) obtain more in-depth information from the research conducted because we can make biological preparations from the animal organs used, (8) obtain maximum data for simulation research purposes, and (9) can be used for safety, diagnostic and toxicity tests. Research that uses experimental animals must use healthy and quality experimental animals in accordance with the research material. These animals are specially bred and raised in a strictly controlled and controlled environment. The aim is to define laboratory animals so that their genotype, phenotype (maternal effect), and type drama (environmental effect on phenotype) are constant. This is necessary so that research is reproducible, that is, it gives the same results if it is repeated at other times, even by other researchers. The use of quality animals can prevent wasting time, opportunity and money.[7,8]

Various small animals have certain characteristics that are relatively similar to humans, while other animals have in common with the metabolic physiological aspects of humans. White rats are often used in assessing protein quality, toxicity, carcinogenicity, and pesticide content of an agricultural food product. Currently, several strains of mice are used in research in laboratory animal experiments in Indonesia, including: Wistar; (originally developed at the Wistar Institute), derivatives of which can be obtained at the Center for Basic Health Technology and the Center for Applied Technology for Health and Clinical Epidemiology of the Litbangkes Agency; and Sprague-Dawley; (albino rats produced on the Sprague-Dawley farm), which can be obtained from the laboratories of the Food and Drug Administration and the Research and Development Center for Basic Health Technology.[9]

Ethics of using experimental animals

The experimental animals used in the research will experience suffering, namely: discomfort, displeasure, distress, pain, and sometimes it ends in death. Based on this, animals that are put forth in research whose results can be utilized by humans should be respected, receive humane treatment, are well cared for, and endeavored to adapt their life patterns as in nature. Researchers who will use experimental animals in health research must examine the feasibility and reasons for using animals by considering the suffering that will be experienced by experimental animals and the benefits that will be obtained for humans.[10]

Principles of research ethics

In conducting research, researchers must create and adapt protocols with scientifically applicable standards and health research ethics. Health research ethics in general are listed in the World Medical Association, namely: respect (respecting the rights and dignity of living things, freedom of choice and desire, and being responsible for themselves, including experimental animals), beneficiary (beneficial for humans and other creatures, benefits obtained must be greater than the risk received), and justice (being fair in using experimental animals). Examples of unfair attitudes include: animals being injected / operated on repeatedly to save the

number of animals, using euthanasia drugs which cause pain due to lower prices.[11,12]

Health research scientists who use animal models agree that experimental animals that suffer and die for the benefit of humans need to be guaranteed their welfare and be treated humanely. In health research that uses experimental animals, the 3 R principles must also be applied in the research protocol, namely: replacement, reduction, and refinement.[13]

Replacement is the need to use experimental animals that have been carefully calculated, both from previous experience and literature to answer research questions and cannot be replaced by other living things such as cells or tissue cultures. Replacement is divided into two parts, namely: relative (replacing experimental animals using animal organs / tissues from slaughterhouses, animals from lower orders) and absolute (replacing experimental animals with cell culture, tissue, or computer programs).[14,16]

Reduction is defined as the use of animals in research as little as possible, but still get optimal results. The usual minimum number is calculated using the Frederer formula, namely (n-1) (t-1)> 15, where n is the number of animals needed and t is the number of treatment groups. The downside of this formula is that the fewer the research groups, the more animals are needed, and vice versa. To overcome this, it is necessary to use appropriate statistical designs in order to obtain valid research results.[15]

Refinement is treating experimental animals humane (humane), maintaining animals properly, not hurting animals, and minimizing painful treatment so as to ensure the welfare of experimental animals until the end of the study. Basically, the principle of refinement means freeing experimental animals from several conditions. The first is to be free from hunger and thirst, by providing access to appropriate food and drinking water in an adequate amount both in quantity and nutritional composition for health.[17] Food and drinking water are of adequate quality, proven through proximate analysis of food, analysis of drinking water quality, and periodic contamination tests. Analysis of animal feed to obtain feed composition, using standard methods. Second, experimental animals are free from discomfort, provided a clean environment and best suited to the biology of the selected experimental animals, with attention to: light cycle, temperature, environmental humidity, and physical facilities such as cage size for freedom of movement, animal habits to group or solitary.[20] Next, experimental animals must be free from pain and disease by carrying out health, prevention and monitoring programs, as well as treatment of experimental animals if necessary.[18] The disease can be treated provided that it does not interfere with ongoing research. Free from pain is attempted by choosing procedures that minimize pain when performing invasive procedures, namely by using analgesia and anesthesia when needed. Euthanasia is carried out by humane methods by trained people to minimize or even eliminate the suffering of experimental animals. Animals must also be free from fear and long-term stress, by creating an environment that can prevent stress, for example providing a period of adaptation / acclimation, providing training in research procedures for animals. All procedures are carried out by personnel who are competent, trained, and experienced in caring for / treating experimental animals to minimize stress. Animals are allowed to express natural behavior by providing space and facilities suitable for biological life and behavior of experimental animal species. This is done by providing a means of social contact (for species of a social nature), including social contact with researchers; placing animals in cages individually, in pairs or groups; provides the opportunity and freedom to run and play.[19] The research protocol should explain in detail the following things: selection, strain, animal origin, acclimatization, maintenance, planned actions, (including actions to alleviate / reduce pain and eliminate animal suffering), the party responsible for animal care, and how to kill, and how to dispose of the cadaver. Description of

treatment in experimental animals can be analogized as informed consent for animals and becomes an assessment in research ethics using experimental animals.[21,22]

2. References

1. Health Research Ethics Committee, Agency for Research and Development. Operational guidelines for the health research ethics commission (PO KEPK). Jakarta: Ministry of Health of the Republic of Indonesia; 2007.
2. National Commission on Health Research Ethics, Ministry of Health, Republic of Indonesia National guidelines for health research ethics supplement II ethics for the use of experimental animals Jakarta: Ministry of Health, Republic of Indonesia; 2006.
3. Guidelines for health research ethics commission (POB) standard operating procedures. Jakarta: Ministry of Health of the Republic of Indonesia; 2011.
4. Oemijati, Setiabudy R Budijanto A. Ethical guidelines for Indonesian medical research. Jakarta: Publisher Faculty of Medicine, University of Indonesia; 1987.
5. 5. Smith JB, Mangkoewidjojo S. Maintenance, breeding and use of experimental animals in the tropics. Jakarta: University of Indonesia Publishers; 1988.
6. Council for International Organization of Medical Sciences (CIOMS) International guiding principles for biomedical research involving animals council for International Organization of Medical Sciences (CIOMS); 1985.
7. 7. Rustiawan A, Vanda J. Biological food quality testing. Bogor: Inter-University Center for Food and Nutrition, Bogor Agricultural University; 1990.
8. Nomura T, Tajima Y. Defined laboratory animals, advances in pharmacology and therapeutics II. Oxford Pergamon Press; 1982.
9. Festing MFW. Principles: the need for better experimental design. Trends Pharmacol Sci. 2003;24:341-5.
10. Herlinda Y. The experimental animal of Wistar strain albino rats in the Diponegoro nutrition research unit. Indonesian Medical Magazine. 1986; 36 (11): 491-495.
11. Marice S, Raflizar. Nutritional status and liver function of CBS-swiss mice) and Wistar white rats in laboratory animal studies, Biomedical and pharmaceutical research and development center, 2010. Health Research and Development Media. 2010; 20 (1): 33-40.
12. World medical association declaration of helsinki : recommendation guiding physicians in biomedical research involving human subject; 1964 Jun; Helsinki, Finland. Amended by 59th WMA,General Assembly, Seoul; 2008.
13. Ball M, Goldberg AM, Fentem JH, Broadhead CL, Burch RL, Festing MF, et al. The three rs: the way forward, the report and recommendation of ECVAM (The European Center for the Validation of Alternative Methods). Altern Lab Anim. 1995; 23(6): 836-66.
14. Russell WMS, Burch RL. The principles of humane experimental technique. London: Methuen & Co. Ltd,1959.
15. Shaw R, Festing MFW, Peers I, Furlong L. The use of factorial designs to optimize animal experiments and reduce animal use.ILAR J. 2002;43:223-32.
16. Bousfield B, Brown R Animal Welfare. Veterinary Bulletin, Agriculture, Fisheries and Conservation Department Newsletter. 2010;1(4):1-12.
17. Horwitz W, editor. Official Methods of Analysis AOAC International. 17th edition. Maryland: Association of Official Analytical Chemists; 2000.
18. Fitzpatrick A. Ethics and animal research. J Lab Clin Med.2003;41:89-90.
19. Insitute of Laboratory Animal Resources Commission on Life Sciences. Guide for the care and use of laboratory animals national academy of science USA National Research Council;2010.

20. Ngatidjan. Pengantar Penelitian Toksikologi. 2000. UGM Press.
21. Gamzu, E., 1985. Animal behavioral models in the discovery of compounds to treat memory dysfunction. Ann. N. Y. Acad. Sci.444, 370–393.
22. Garattini, S., 1997. Alternatives to animal experiments: expectations and limitations. In: van Zutphen, L.F.M., Balls, M. (Eds.), Animal Alternatives, Welfare and Ethics. Elsevier, Amsterdam, pp. 55–66.