

Japanese regulation of laboratory animal care with 3Rs

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Abstract

In Japanese Law for the Humane Treatment and Management of Animals defines animal experimentation as the use of animals for scientific purposes with the consideration of 3Rs. Under the Law, Standard Relating to the Care, Management and Pain and Distress Alleviation of Laboratory Animals regulates the usage of laboratory animals in Japan. However the animal experimental procedures will be promoted appropriately with the understanding of the people but not legal restriction. In Japan laboratory animal care is regulated but the conduct of animal experimentation is not. The various ministries notice the research organizations to establish self regulated system in animal experimentation. The Science Council of Japan recently published Guidelines for Proper Conduct of Animals Experiments (The Guide). The Guide was published much alike ILAR Guide in USA. It says that the director of institutions a person with overall responsibility in the institution for proper and safe conduct of the animal experiments. It recommends establishing in-house regulations specified for the proper conduct of animal experiments. The Guide also defines the task of IACUC as advisory body to the director of the institution and their activities. The emphasis of the Guide is the protocol review by IACUC.

Keywords: Japanese regulation, animal experimentation, laboratory animal welfare, laboratory animal care, 3Rs principle

Introduction

There are several laboratory animal welfare regulations in Japan. However it is fairly difficult for foreigners to understand the regulatory system in laboratory animal welfare in Japan due to the language barrier. The most of Laws and Standards are written in Japanese and the formal translation of these is not available. After the recent revision of the Law and Standard in 2005 to 2006, the translation to English of relevant articles are published such as Fundamental Guidelines for Proper Conduct of Animal Experiment and Related Activities in Academic Research Institutions under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology as Ministry of Education, Culture, Sports, Science and Technology, Notice No. 711¹⁾ and Guidelines for Proper Conduct of Animal Experiments by Science Council of Japan (the Guide)²⁾

This article describes to clarify the Japanese regulatory system in laboratory animal welfare.

Regulatory system of laboratory animal care Japanese regulatory system in laboratory animal welfare has a hierarchy.

The upper most regulation is the Law. "the Law for the Humane Treatment and Management of Animals (Law No. 105, 1973)" which was revised several

times and the most recent revision was made in 2005 (Table 1).

The Law

The Law says in its fundamental principles; Article 2

Because animals are living beings, all people are required not only to avoid purposeless killing, injuring, and afflicting animals, but also to treat animals properly while taking the need for symbiosis between people and animals and the natural habits of animals into account.

If one will follow the Law, it is very difficult to conduct animal experimentation in Japan because

Table 1. Japanese regulation on laboratory animal welfare

• the Law for the Humane Treatment and Management of Animals (the Law)
• Standard Relating to the Care, Management and Alleviation of Pain and Distress of Laboratory Animals (the Standard)
• Various Guidelines
–Ministry of Education ¹⁾
–Ministry of Health
–Ministry of Environment
–Ministry of Agriculture and Fisheries
–The Science Council of Japan
• (The Guide) ²⁾
• Institutional rules in animal experimentation

all people are required to avoid killing, injuring and afflicting animals. It is almost impossible to conduct animal experimentation without the killing, injuring and afflicting animals. However if we can read the Law carefully, we can recognize that the Law says the avoidance of purposeless killing of animals. We are allowed to conduct the purposeful animal experimentation under the Law in Japan. In fact, the Law regulates "Methods When Animals are Used for Scientific Purposes and Subsequent Disposal of Such Animals" in article 41 and section 2 says "Where an animal is used for the purposes of education, testing, manufacture of biological products or other scientific purposes, it shall be so used by methods that cause the animal minimum pain and distress possible within the limits imposed by the purposes."

The section 1 of article 41 of the Law was added at the revision made in 2005. The section 1 says replacement; the application of alternative methods that do not require the use of animals within limits that allow scientific objectives to be achieved, and reduction; the use of as few animals as possible within limits that allow scientific objectives to be achieved.

The Law requires us 3Rs when we are conducting animal experimentation and the animal experimentation should be purposeful.

The standard

Under the Law, the Standard is amended. There are four standards in animal welfare and one guide under the Law in Japan. The animals are categorized in four sections such as house hold animals (pet animals), exhibition animals (zoo animals), farm animals and experimental animals. Each categorized animals has its standard. One guide under the Law is for methods of euthanasia.

The standard for laboratory animal welfare is "Standards Relating to the Care and Management, and Alleviation of Pain and Distress of Experimental Animals" as Notice No. 6 of the Prime Minister's Office 1980 and the most recent revision was made in 2006. The previous title of the Standard was just for the care and management of experimental animals but the alleviation of pain and distress was added to the title of the Standard at the recent revision.

The Standard says; Usage of animals for scientific purpose is necessary and indispensable for the advancement of biomedical science and the development of medical technology. However the 3Rs should be considered when animals are used for scientific purposes.

In the Japanese regulatory system in laboratory animal welfare, the animal experiments are positively supported for the advancement of biomedical science and the development of medical technology. However the laboratory animal care and management

are regulated by the Standard. The article 3 in the Standard describes six sections namely, 1, Health and Safety of Animals, 2, Maintenance of life environment (of man), 3, Prevention of harm (of man), 4, Training in zoonosis, 5, Record keeping of animals, 6, Transportation of animals. The Standard is not only for animal welfare but also for human welfare (public hygienic aspects).

The article 4 of the Standard regulates animal procedures too. The section 1 of the article 4 regulates various aspects (Table 2).

When the revision of the Law was made in 2005, the government officials explain that the animal experiments and animal care might be different. The former is a part of research activities and the academic freedom should be protected. Therefore the animal experiments itself is not the matter to be regulated by the law. However the later should be regulated in the regulatory system such as the Standard.

Because the article 4 of the Standard regulates the animal experimentation shown in Tables 2, the Standard is thought to regulate the animal experiment itself. The explanation of the government officials may be in difficulty.

Table 2. The section 1 of article 4 of the Standard

1. Animal Research Facilities
<ul style="list-style-type: none"> • Consider good experimental procedures • Appropriate usage of animals • Purposeful experimental procedures • Administration of anesthetics and analgesics • Shorter duration of procedures • Minimize pain and distress • Euthanasia with overdose of anesthetics
2. Animal Breeding Facilities

Guidelines

The recognition of the government officials on animal experimentation and laboratory animal care, the animal experiments should not be regulated by the Law but the voluntary system which may regulate the conduct of animal experimentation under the responsibility of researchers. After the revision of the Law, various ministries made notices for the proper conduct of animal experiments in their research institutions. In Japan the most advanced biomedical research institutions are universities which is under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology. Because the guidelines of various ministries are not different very much, the guidelines by the Ministry of Education, Culture, Sports, Science and Technology is explained in this article.

The guideline emphasizes Responsibilities of the director of the academic research institution in article 2 and IACUC establishment in article 3 and 3Rs in article 4. Before the guideline was published, the responsibility for the laboratory animal welfare was

Table 3. Index of Fundamental Guidelines for Proper Conduct of Animal Experiment and Related Activities in Academic Research Institutions under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology

Preamble
Article 1 Definition
Article 2 Responsibilities of the director of the academic research institution
<ol style="list-style-type: none"> 1. Responsibilities of the director of the academic research institution 2. Establishment of institutional regulations 3. Approval of animal experiment protocols 4. Comprehension of the results of the animal experiment and related activities.
Article 3 Institutional Animal Experiment Committee
<ol style="list-style-type: none"> 1. Establishment of the Institutional Animal Experiment Committee 2. Roles of the Institutional Animal Experiment Committee 3. Membership of the Institutional Animal Experiment Committee <ol style="list-style-type: none"> (i) Individuals with excellent knowledge and experience regarding animal experiments and related activities. (ii) Individuals with excellent knowledge and experience regarding laboratory animals. (iii) Individuals with scholarship and experience.
Article 4 Conduct of animal experiments and related activities
<ol style="list-style-type: none"> 1. Assurance of scientific rationale <ol style="list-style-type: none"> (1) Selection of proper methods for the animal experiment and related activities <ol style="list-style-type: none"> (i) Use of alternative methods (Replacement) (ii) Selection of laboratory animals (Reduction) (iii) Reduction of pain (Refinement) (2) Facilities and equipments for animal experiment and related activities 2. Animal experiments and related activities that require special attention concerning safety management
Article 5 Rearing and maintenance of laboratory animals
Article 6 Miscellaneous Provisions
<ol style="list-style-type: none"> 1. Conduct of education and training 2. Self-inspections, evaluation and verification of compliance with the Fundamental Guidelines

not clear. In some of universities apart from medical schools, there were no IACUC. Naturally, some of research investigators did not know 3Rs principles in laboratory animal welfare.

The Guide²⁾

Before the revision of the Law, some of laboratory animal specialists recognized the difference between Japanese and westerns countries in laboratory animal welfare regulatory system. Their main concerns are the paucity of the standardized guide in laboratory animal care and use in Japan. Specialists in Science Council in Japan have published Guidelines for Proper Conduct of Animal Experiments (the Guide)²⁾.

The guide says in the preamble "the rationalization of animal experimentation was based on administrative guidance rather than laws and regulations because of its importance in the advancement of scientific research.²⁾". This might be the reflection of the statement of government officials in laboratory animal welfare in Japan. In the preamble, the Guide summarizes the past progress of scientific research in Japan as follow; "As a result, it became possible to conduct highly creative scientific research in a free and open manner and Japanese medicine and life sciences made remarkable progress on an international level.". The Guide recommends "For progress in life science, it is recommended to have a voluntary system of animal experimentation

under the responsibility of researchers who best understand the necessity of such experimentation.". After the recommendation the Guide concludes "Handling of laboratory animals is influenced by the religion and culture of each country.", "The so-called North American model specifies voluntary management of animal experimentation without relying on legal restrictions on scientific procedures." and "while Japan favors the establishment of a system based on Japanese customs.". The intention of the publication of the Guide is that the publication of Japanese national guide for the conduct of animal experimentation similar to the ILAR guide³⁾ or CCAC guide⁴⁾.

One who checked the index of the Guide (Table 4) can recognize the similarities of the headings of the ILAR guide³⁾. The ILAR guide consists of 4 chapters namely 1, Institutional policies and responsibilities, 2, Animal environment, housing and management, 3, Veterinary medical care and 4, Physical plant. The clear difference between these two guides is in veterinary medical care. The ILAR guide emphasizes the importance of veterinary medical care but not the Guide in Japan.

There are several differences between ILAR guide and the Guide. The careful analysis of the comparison of these two guides may be necessary.

However the recognition of the reality of animal experimentation in Japan is more important than the

Table 4. Index of Guidelines for Proper Conduct of Animal Experiments by Science Council of Japan (The Guide)²⁾

Basis and objectives	
No.1	Definitions
	<ul style="list-style-type: none"> 1) Animal experiment 2) Facilities 3) Laboratory animal 4) Institution 5) Director of institution 6) Animal experiment protocol 7) Researcher(s) 8) Principal investigator 9) Manager 10) Laboratory animal manager 11) Animal technician 12) Manager, etc. 13) Policies 14) Regulations
No. 2	Responsibility of the director of the institution
No. 3	Institutional Animal Care and Use Committee 1) Roles of the Institutional Animal Care and Use Committee 2) Institutional Animal Care and Use Committee organization
No. 4	Animal experiment protocol drafting and experimental procedures
	<ul style="list-style-type: none"> 1 Drafting of animal experiment protocol <ul style="list-style-type: none"> 1) Items requiring consideration when drafting an animal experiment protocol 2) Animal experiment protocol form 2 Experimental procedures <ul style="list-style-type: none"> 1) Laboratory and laboratory equipment 2) Animal restraint 3) Food and drinking water restrictions 4) Surgical procedures 5) Analgesic procedures, anesthetics and postoperative management 6) Humane endpoint 7) Euthanasia procedures 8) Safety management considerations 9) Reports of animal experiment results
No. 5	Laboratory animal selection and receipt
	<ul style="list-style-type: none"> 1) Introduction of laboratory animals 2) Quarantine and acclimatization 3) Transport 4) Provision of information on delivery and receipt of laboratory animals
No. 6	Care and management of laboratory animals
	<ul style="list-style-type: none"> 1) Fundamentals of care and management 2) Cage environment and animal room environment <ul style="list-style-type: none"> (1) Housing space (2) Environmental temperature and humidity (3) Ventilation (4) Lighting (5) Food (6) Water 3) Retention of records
No. 7	Laboratory animal health management
No. 8	Facilities
No. 9	Safety management
	<ul style="list-style-type: none"> 1) Understanding and dealing with risk factors 2) Prevention of injury by laboratory animals 3) Measures when laboratory animals escape 4) Dealing with emergencies 5) Maintenance of the living environment
No. 10	Education and training
No. 11	Others

analysis of the Guide for laboratory animal welfare. Under the Guide, we should expect the improvement of laboratory animal welfare in Japan.

Conclusion

The Law of animal welfare in Japan was revised in 2005. The Standard of laboratory animal welfare and the guidelines of various ministries and science council Japan are published. Under these circumstances, the research institutions in Japan are expected to implement the 3Rs policies for their animal experimentation. Because the scientific activities including alternative research should be international, laboratory animal welfare should be harmonized internationally to conduct fair scientific activities. Japanese regulatory system in laboratory animal welfare may not be harmonized with the international standard yet. Japanese should regulate animal experimentation as they do in advanced countries on the basement of 3rs principles.

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