A Draft Amendment to “the Law for the Humane Treatment and Management of Animals” and “Standards Relating to the Care and Management etc. of Experimental Animals” in Japan

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In 1973, the Law Concerning the Protection and Control of Animals was enacted, to become the basic law in Japan covering all animals (hereinafter called “the old animals law”). Article 4, Paragraph 2 of the old animals law set forth the policy that the Prime Minister may, after consultation with the heads of the administrative organs concerned, prescribe standards applicable to the care and custody of animals. Pursuant to this provision, the Standards Relating to the Care and Management etc. of Experimental Animals (hereinafter called “the Experimental Animals Standards”) were promulgated in 1980. However, since the Experimental Animals Standards did not include adequate regulations concerning animal experiments, in 1987 the Head of the Science and International Affairs Bureau of the Ministry of Education issued a notice on animal experiments in universities, to nationwide national, public and private universities, etc. In response to this notice, Japanese universities prepared the Guidelines for Animal Experiments. Later, in 2000, the old animals law was amended and renamed “the Law for the Humane Treatment and Management of Animals” (hereinafter called “the new animals law”). This new animals law, however, did not include amendments of the old animals law’s provisions pertaining to experimental animals and animal experiments, simply stating that the law would be reviewed in 5 years after enactment.

Current Japanese regulations on animal experiments can be characterized by the greater role played by the Guidelines for Animal Experiments prepared voluntarily by individual universities, than by the new animals law or the Experimental Animals Standards prepared by the central government. The protocols, place, etc., for animal experiments conducted by investigators are now checked voluntarily by an institutional review board (the animal experiment committee) organized in accordance with the Guidelines for Animal Experiments of universities. About 15 years have elapsed since, in about 1988, the Guidelines for Animal Experiments were prepared at various institutions. To date, the system for inspecting study protocols and facilities at the animal experiment committee of individual institutions has become broadly accepted. However,
these voluntarily controls by animal experiment committees present such problems as lack of legally binding force, lack of surveillance by administrative organs (relying too much on scientists' voluntary control) and discrepancies in the extent and methods of voluntary control among different universities and other facilities.

Under these circumstances, we thought it necessary to amend both the new animals law and the Experimental Animals Standards, particularly those parts related to animal experiments. Based on this view, we studied what amendments of these law and standards should be made. We reached the conclusion that, while the conventional basic policy of voluntary control of animal experiments by universities, should be retained, these law and standards should be amended to introduce new regulations. These would pertain to the obligation of those planning animal experiments to report the facilities and management systems of animal experiments to administrative organs and the obligation and requirements related to the animal experiment committee and the procedure of planning animal experiments. We thus drafted a revised law and set of standards. During my speech, I will present the history leading up to the proposal of these draft amendments of the new animals law and the Experimental Animals Standards, and the contents of these drafts. I think that when establishing appropriate animal experiment practices, as indicated by the title of this speech on the basis of introducing these new regulations, it is essential to devise a method for correcting discrepancies in methods and degrees of voluntary control among different universities or other facilities. One valid solution to this issue may to introduce a third party surveillance system, like the US system called AAALAC. The members of the symposium invited here today were selected on the basis of such a premise.
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### 1. Preface

#### 1.1 Purpose

This Guideline is designed to stipulate the matters to be observed in planning and conducting animal use by the National Space Development Agency of Japan (NASDA) or any animal use supported by NASDA, as well as to stimulate appropriate conduct of all such research activities using animal subjects, under the related laws and regulations of Japan and the NASDA Regulations for Animal Care and Use, for contributing to improvements in...
1.4.6 Animal Facility Manager
The Animal Facility Manager is the person who is charged with the responsibility for maintaining and managing animal facilities.
The Animal Facility Manager at NASDA shall be appointed in accordance with the pertinent NASDA regulations. The Animal Facility Manager at any external (non-NASDA) organization shall be appointed in accordance with the regulations of the said organization.

2. Duties and Responsibilities

2.1 Animal Care and Use Monitoring
2.1.1 System Office Director
Based on IACUC reports, the Director of the Office of Space Utilization Systems (hereinafter referred to as the "System Office Director") shall evaluate and supervise animal experimental plans, experimental procedures, and animal care/use facilities at NASDA that should conform to the related laws and regulations of Japan, NASDA Regulations for Animal Care and Use, this Guideline, other applicable guidelines, etc. The Chair and members of the IACUC shall be appointed or commissioned by the System Office Director. The System Office Director is accountable for facilitating the conduct of education and training, the maintenance of equipment, supply of information, and the like so as to ensure the appropriate care and use of animals pertaining to NASDA. This duty may be entrusted, where required, to the System Office Vice-Director, the Director of the Space Utilization Research Center (hereinafter referred to as "Center Director"), or any other person deemed necessary. Animal use conducted at a non-NASDA facility(-ies) in the event of a cooperative or contracted research project may follow the regulations of the relevant external organization at the discretion of the IACUC. The responsibility for the care and use of animals conducted by NASDA lies with the "System Office Director".

2.1.2 Institutional Animal Care and Use Committee
The System Office Director shall designate a Chairperson of the Institutional Animal Care and Use Committee (IACUC) from among NASDA officials who possess extensive knowledge and experience of life science experimentation including space experiments and animal use. The numbers of other members of the Committee shall be five or more including experts in laboratory animal science, those in laboratory animal use, veterinarians, persons with experience and expertise, etc., of whom at least two members should be currently unaffiliated with NASDA. The Institutional Animal Care and Use Committee shall be operated by the Space Utilization Research Center.

2.1.2.1 Activities
The Institutional Animal Care and Use Committee shall review animal experimental plans in compliance with the related laws and regulations of Japan, NASDA Regulations for Animal Care and Use, this Guideline, other applicable guidelines, etc., and shall approve only those projects deemed to be appropriate upon consideration of the balance between the scientific validity of the project and the welfare of the animals used therein. The Institutional Animal Care and Use Committee shall, on commission of the System Office Director, monitor the projects and inspect the facility(-ies) where the animal use are conducted. Further, the Committee shall suggest points to be improved/modified regarding animal use, facilities/equipment involved in the animal use, NASDA regulations relevant to laboratory animals and animal use and this Guideline. The Chairperson of the Institutional Animal Care and Use Committee shall report the outcome of review and inspection or suggestions for improvements/modifications to the Center Director, who shall then report them to the System Office Director. The Institutional Animal Care and Use Committee is duty bound to cooperate in the instruction, training, maintenance of equipment, supply of information, etc. conducted on the authority of the System Office Director for promoting the appropriate care and use of animals at NASDA.

2.1.2.2 Review of Animal Experiment Protocols
In principle, reviews at the Institutional Animal Care and Use Committee shall be document reviews based on animal experiment protocols. The items to be included in the protocol shall be determined by the IACUC. The IACUC may require the Principal Investigator to provide further information necessary for the review, e.g., research protocol. The IACUC can proffer advice at the request of the Principal Investigator.
In the event that there is a request for improvement from the viewpoint of occupational safety and hygiene as a result of an IACUC inspection, the Animal Facility Manager must deal with the matter appropriately.

2.3 Safety Management
Animal use requiring special precautions in securing safety management include those involving the use of recombinant DNAs, radioisotopes or hazardous drugs/poisons and those using pathogenic organisms. Such work should be performed in compliance with the regulations set forth separately for respective categories.

2.4 Consideration for Environment
2.4.1 Disposal of Wastes
Disposal of wastes that is generated in association with the use of animals should be carried out in accordance with all related laws, regulations, guidelines and other rules applicable to animal facilities.

2.4.2 Animal Facility and Surrounding Environment
Considerations for the animal facility and surrounding environment are of significance to the use of animals. For example, it is essential to implement measures for hygienic control, control of physical factors such as noise and odors at the animal facility, and prevention of escape by the animals from the facility.

2.4.3 Maintenance of Ecosystems
Undue destruction of ecosystems attributable to animal use must be avoided. In the event where, for example, wildlife (inclusive of plants) is to be collected for animal use, due consideration should be given to the potential impact of the collection on the ecosystem.

2.5 Education and Training
The care and use of animals pertinent to NASDA shall be conducted by persons who are adequately qualified and/or who have sufficient knowledge and appropriate experience. The System Office Director shall endeavor to promote instruction and training aimed at improving the welfare and techniques related to animal handling at NASDA, to maintain appropriate reference data within NASDA, and to provide information where necessary.

3. Animal Housing Environment, Accommodation and Management

3.1 Animal Environment and Management
3.1.1 Physical Environment
Animal facilities should be maintained within suitable ranges of the following physical environmental factors for the species to be accommodated:
- ambient temperature and humidity
- water temperature and water quality control (aquatic animals, etc.)
- ventilation, air flow, wind velocity, and dust
- lighting
- noise and vibration
- housing space (floor space, vertical space, separation from different species)
- housing system (type of cages, number of animals housed per cage, feeding and watering methods, etc.)

3.1.2 Behavioral Management
The animal care should be in accordance with the propensities of the species being accommodated, and consideration of the following points relating to animal behavioral management should be given:
- social environment (direct and indirect inter-animal contact, i.e., communication)
- activities (characteristic posture and motions peculiar to species)

3.1.3 Husbandry
Effort should be made to ensure animal welfare, safety and health, taking into account the following points for animal husbandry:
- diet and drinking water

The Principal Investigator should collect sufficient information and select analgesics and anesthetics and their doses that are ethically and clinically optimal without marring the scientific significance of the research.

4.5 Euthanasia
Euthanasia is the practice of inducing a rapid loss of consciousness and death in animals while controlling pain and distress to the minimum. The procedures and drugs used for euthanasia should be selected in accordance with the species and the objectives of research. The Principal Investigator should collect sufficient information and, thereby, select euthanizing procedures that are ethically and clinically optimal without marring the scientific significance of the research (it is generally considered to be preferable to administer drugs {e.g., barbiturates, non-explosive anesthetics, carbon dioxide} by inhalation or injection, as opposed to the use of any physical methods {e.g., cervical dislocation, decapitation, electroshock}). In principle, euthanasia should be performed by properly trained personnel, and the death of the animal must be confirmed by a person capable of judging the cessation of vital activities.

5. Space Experiments and Ground-Based Preliminary Research

5.1 Space Experimentation Plan
For space experiments involving animal handling and related ground-based experiments (e.g., aboveground preliminary experiments, aboveground control experiments, post-flight analysis), the research team must include veterinarian(s) or laboratory animal expert(s), and the Principal Investigator shall plan the experiment upon deliberate consultation with the veterinarian(s) or the laboratory animal expert(s). In the event where two or more individually approved plans are to be consolidated, the plan shall be adjusted among the IACUCs at which the individual plans have been reviewed and, where necessary, the Principal Investigator of the consolidated project shall re-submit the unified plan for review.

5.2 Space Experimentation
Every use of laboratory animals to be conducted on board spacecraft shall be subject to IACUC approval. The method and significance of each procedure on the animals should be clearly established prior to the experiment while taking into account the method of transportation and that of animal husbandry practices at space-related facilities. Since actual space experiments will be basically be conducted through international collaboration, it is important to make prior adjustment among the countries concerned.

5.3 Inherent Ground-Based Experiments Related to Space Experimentation
The following are precautions for major experimental methods inherent to space experiments:

5.3.1 Aircraft experiments
Precautions must be taken with respect to the animal transport method, animal procurement, animal care on site, restraint methods on board aircraft, and stress-driven behavior that may be caused by microgravity or hypergravity.

5.3.2 Drop Tower Experiments
Caution must be exercised in conjunction with the animal transport method, animal procurement, animal care at site, method of restraint in a drop capsule, and the impact of dropping. Care should also be taken to secure ventilation in the drop capsule.

5.3.3 Simulated Microgravity Experiments
In various simulated microgravity experiments such as tail suspension experiments, caution must be exercised to whether continuation of such testing inflicts any physical injury or poses excessive stress on the animals, and the behavior or health status of the animals should be observed and recorded daily. The experiment should be immediately discontinued if the animal becomes anorectic and incapable of drinking water.

5.3.4 Hypergravity Experiments
As per Section 5.3.3.
Guidelines for Animal Experimentation

Nagasaki University

Decision of the University Council
December 22, 1989

Animal experiments have made a great contribution to the formation and advance of human culture, and will continue to do so in the future. Their contribution to natural science has been especially remarkable. However, animal experiments should be conducted taking into consideration the maintenance of animal welfare from the basic viewpoint that the life of animals should be respected, but, at the same time, fulfilling various experimental requirements so that reproducibility, which forms the basis of objective results and evaluations, can be obtained by conforming to the general principles of scientific research.

The necessity of thoughtful consideration for animal welfare has been specified in the “Law Concerning the Humane Care and Control of Animals” (Law No. 105, October 1, 1973) and in “Standards Relating to the Care and Management, etc. of Experimental Animals” (Notification No. 6, 1980, by the Prime Minister’s Office); and furthermore, this necessity has been stated specifically in connection with animal welfare and animal experimentation in the recommendation entitled “Concerning the Establishment of Guidelines for Animal Experimentation” resolved at the 80th General Assembly of the Science Council of Japan and in the report named “Concerning the Basic Policy of the Performance of Animal Experimentation in Universities, etc.,” issued by the Scientific Data Section of the Scientific Information and Data Subcommittee, Science Council.

Nagasaki University lays down the Guidelines for Animal Experimentation, duly recognizing the fact the animal experiments performed by researchers of the University should conform to these basic principles.

1. (Purpose)

The purpose of the Guidelines is to prescribe matters to be observed at the time of planning and executing animal experiments at Nagasaki University (hereafter called “the University”) so that experiments can be conducted properly not only from a scientific viewpoint but also from an ethical one with due consideration for animal welfare.

2. (Range of Applications)

1. The Guidelines should be applied to all experiments conducted at the University using mammals and birds.

2. In addition to the preceding paragraph, it is to be desired that experiments using animals other than mammals and birds should be conducted in adherence to the spirit of the Guidelines.
3. (Basic Principle)

Persons who conduct animal experiments (hereafter called “investigators”) should take responsibility for entire experiments including formulation of experimental plans, execution of experiments and adoption of necessary post-experimental measures, and pay close attention to the maintenance of proper experimental environments.

4. (Consolidation of Facilities, Equipment and Organizational Structure)

1 Sections properly equipped for the right and smooth execution of experimental animal care and animal experimentation (hereafter called “exclusive sections”) should be secured.

2 Appropriate facilities for the care and use of animals in experiments should be established taking into consideration the habits, ecology, etc. of the animals.

3 The deans in whose faculties, etc. conducting animal experiments should endeavor to consolidate experimental facilities, equipment and the organizational structure necessary for the management and operation of them.

5. (Matters that Require Attention Concerning Experimental Plans)

1 Investigators should refer to literature, etc. when planning animal experiments, and endeavor to refrain from experiments conducted for the mere reconfirmation of established facts.

2 Investigators should formulate experimental plans after making a close examination of respective research purposes and take into careful consideration of the presence of any possible alternatives to animal experiments.

3 Investigators, when selecting animals suitable for experimental purposes, should take into account their species, strain, quality, number and the conditions of their care and use in experiments, in order to reduce the scope of animal experiments to the minimum necessary for the achievement of research purposes.

4. Investigators should also give careful attention to the methods and environments of experiments from an ethical viewpoint, endeavoring; for instance, to alleviate as much as possible the anguish inflicted on animals, throughout experiments.

5. Investigators, when formulating experimental plans, should check each of the items in the annexed list. In addition, investigators should, in case of need, seek the advice from experts who have substantial knowledge and experience in laboratory animals or animal experimentation (hereafter called "experts").

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6. (Application and Approval Concerning Animal Experimental Plans)

1. Investigators should draw up written experimental plans in due form prescribed by the Animal Care and Use Committee, Nagasaki University (hereafter called "the Committee"), organized according to the provision of Paragraph 1, Article 15; and apply it to the President through the deans in whose faculties, etc.

2. When written experimental plans are applied, the President should refer the applications to the Committee for inspections.

3. In the process of the inspections, the Committee may devise necessary measures for approval to investigators such as providing advice, or making them revise the written experimental plans.

4. On receiving the results of the Committee's inspections, the President should determine to give an approval or not to each, and notify the decisions promptly to the investigators through the deans in whose faculties, etc.

5. The Committee may request investigators to present reports on the progress of the experiments approved by the President as occasion demands.

6. The President may prohibit or urge to abandon the experiments, according to the experimental circumstances, in compliance with the Committee's request.

7. (Modifications of the Experimental Plans)

These regulations on Article 6 apply to cases of modifications of experimental plans.

8. (Report on Closing or Cancellation of the Experiments)

In case investigators close or cancel experiments, they should submit the report of closing or cancellation of experiments, in due form prescribed by the Committee, to the President through the deans in whose faculties, etc.

9. (Introduction of Experimental Animals into Facilities and Quarantine Work)

1. Investigators should not only confirm the conditions of orders given for animals and the presence of abnormalities or deaths, but also record the state of animals and the means and time of transportation, etc. when the animals are introduced into facilities.

2. Investigators should quarantine experimental animals when they are brought in. However, investigators may substitute certificates of genetical and microbiological quality issued by animal breeders for a part of quarantine work, in case the breeders are highly reliable.
3. Investigators should check the result of quarantine work; and, in case abnormalities are found in some animals, they should take proper measures and avoid using the abnormal animals until the abnormalities have become extinct.

4. Investigators should endeavor to acclimatize animals to new environments, as occasion demands.

5. Investigators may seek the advice or cooperation from experts regarding the confirmation and records prescribed in Paragraph 1, the quarantine work prescribed in Paragraph 2, and the measures prescribed in Paragraph 3.

10. (Care and Rearing of Experimental Animals)

1. Investigators should make a close observation of the state of animals all the time from the introduction until the completion of experiments and take proper measures in case the situation demands.

2. Investigators should endeavor to maintain and manage exclusive sections and facilities for animal rearing and experimentation. To secure this, investigators should pay attention to physico-environmental factors – atmospheric conditions (temperature, humidity, air-flow, wind velocity, ventilation, light, smell, dust, etc.) of animal rooms and laboratories; living conditions (structure of animal rooms, cages, bedding, feeding, watering, etc.); sound and vibration, etc. – and bio-environmental factors – animal-room inmates (species, strain, sex, age, number, density of animal population, etc.); microbiological contamination; unnecessary addition of stress; etc.

3. Investigators should endeavor to attend to the care and rearing of experimental animals, supplying food, water, etc. in an appropriate manner.

4. Investigators may seek the advice or cooperation from experts regarding the care and rearing stipulated in the three preceding paragraphs.

11. (Access to Exclusive Sections)

Persons other than investigators, experts and others related to experiments ought to, as a principle, refrain from entering exclusive sections.

12. (Experimental Procedures)

1. Investigators should take care not to inflict unnecessary anguish on animals by using proper restraints and anesthetics.

2. Investigators should seek the advice from experts in matters prescribed in preceding paragraph as occasion demands.
13. (Measures to Be Taken after Experiments, etc.)

1. When disposing of experimental animals on which experiments have been concluded or discontinues investigators should endeavor to release the animals from anguish immediately by administration of a lethal dose of an anesthetic, cervical dislocation, inhalation of carbon dioxide, or other proper means of euthanasia.

2. Investigators should endeavor to prevent environmental pollution by the carcasses, etc., of experimental animals.

3. Investigators may seek advice or cooperation from experts regarding the measures prescribed in preceding two paragraphs.

14. (Animal Experiments using Hazardous Substances, etc.)

1. Animal experiments using pathogens or recombinant DNA should be under the application of “Regulations Concerning the Prevention of Biohazards, Nagasaki University” (Regulation No.14, 1983) or “Regulations Concerning the Safety Control of Recombinant DNA Experimentation, Nagasaki University” (Regulation No.15, 1983) respectively.

2. Animal experiments using radioactive substances and radiation should be under the application of “Radiations Concerning the Safety Control of Radioisotopes and Radiation, Nagasaki University” (Regulation No.12, 1976) and “Regulation Concerning the Prevention of Radiation Injury by X-ray Units for Educational and Research Purposes, Nagasaki University” (Regulation No.16, 1983).

3. When conducting animal experiments using hazardous substances for carcinogenicity or mutagenicity tests, etc, or other substances whose safety is not yet confirmed, or hazardous substances to the environment, investigators should take appropriate measures to prevent the contamination of the environments and other experimental animals.

4. Investigators should seek advice from experts, or submit plans to the Committee for deliberation in case of designing animal experiments using hazardous substances.

15. (Setting up the Committee)

1. The Animal Care and Use Committee, Nagasaki University shall be organized in order to enforce the Guidelines in an appropriate manner as well as to examine animal experiments applied by investigators are conformable to the Guidelines.

2. The items necessary for the operation of the Committee (prescribed in preceding Paragraph 1) shall be prescribed elsewhere.
Supplementary Provision  (Decision of the University Council, July 13, 2001)

The Guidelines shall come into force from October 1, 2001.

Annexed List

1. Environmental conditions of exclusive sections
2. Duration of animal experiments
3. Conditions for the introduction of animals into facilities
4. Experimental animals used: species; strain; genetical and microbiological quality; sex; age; number; etc.
5. Methods of experiments: administrative; sampling; observational; surgical; etc.
6. Methods used for the alleviation and elimination of animal's anguish: kinds and doses of anesthetics/analgesics, etc.; methods of administration; restraints; etc.
7. Methods of animal disposal after experiments: euthanasia; etc.
8. Preventive procedures against any possible inter-animal and environmental contamination by physically; chemically, and biologically hazardous substances used for animal experiments
9. Reasons for the necessity of animal experiments (Reasons for not using alternatives to animal experiments)