(動物実験の適正な実施に向けたガイドライン)

Guidelines for Proper Conduct of Animal Experiments

June 1,2006

Science Council of Japan

Preface

The necessity of basic considerations for the handling of laboratory animals in Japan had been based on the Law for the Humane Treatment and Management of Animals (Law No. 105, 1973) and Standards Relating to the Care and Management of Experimental Animals (Notice No. 6 of the Prime Minister's Office 1980).

Under these conditions, the rationalization of animal experimentation was based on administrative quidance rather than laws and regulations because of its importance in the advancement of scientific research. The Science Council of Japan submitted a recommendation to the government in 1980 entitled "Establishment of Animal Experimentation Guidelines." In response to this recommendation, the Ministry of Education issued a notification to related institutions entitled "Animal Experimentation in Universities and Similar Institutions, etc." (Director General, Science and International Affairs Bureau, 1987). Based on this notification, research institutions established policies for more appropriate conduct of animal experiments and Institutional Animal Care and Use Committees, and applied them in detail. 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.

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. There are also calls for the exercise of government authority in animal experimentation. Therefore, establishment of guidelines on animal experimentation became an urgent necessity and Subcommittee 7 of the Science Council of Japan issued a proposal entitled "Promotion of public understanding of animal experimentation" in 2004.

On receipt of this proposal, the Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labor and Welfare compiled "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" and "Basic policies for the conduct of animal experimentation in the Ministry of Health, Labor and Welfare." The two ministries requested the Science Council of Japan to prepare general guidelines to serve as a model when research institutions compile their own specifications for animal experimentation in accordance with the above fundamental guidelines and basic policies.

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, while Japan favors the establishment of a system based on Japanese customs. With such a system, it is always hoped that animal experimentation will be promoted appropriately with the understanding of the people and will contribute to advances in life science research.

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Basis and objectives

Animal experiments are indispensable in medical and life science education, research and testing. They should be managed and conducted voluntarily under the responsibility of each research institution. The researcher must draft the animal experiment protocol based on scientific rationale and also should consider the welfare of the animal. The researcher must have the Institutional Animal Care and Use Committee review the suitability of the proposed animal experimentation protocol when conducting an animal experiment.

These Guidelines were prepared with the objective of appropriate implementation of animal experiments from a scientific standpoint in accordance with fundamental

quidelines and basic policies on the conduct of animal experiments formulated by government organizations with jurisdiction over institutions conducting animal experiments (Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labor and Welfare, etc.) ("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" Notice of the Ministry of Education, Culture, Sports, Science and Technology dated June 1, 2006 and "Basic policies for the conduct of animal experiments, etc. in the Ministry of Health, Labor and Welfare," Notification of the Ministry of Health, Labor and Welfare dated June 1, 2006). The handling of laboratory animals is specified in "Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain" (Notice No.88 of the Ministry of Environment dated April 28, 2006).

These Guidelines consist of chapters on the responsibility of institutions concerning voluntary management and the Institutional Animal Care and Use Committee at the beginning followed by chapters on procedures for animal experiments and selection of laboratory animals. These are followed by care and management of laboratory animals, health management, facilities and occupational health, education and training required for appropriate animal experiments, self-inspections and evaluations, validation and publication of information.

Each institution should formulate voluntary in-house regulations for proper scientific conduct of animal experiments based on these Guidelines.

Note: These Guidelines are not intended for application in education, research or testing aimed at improvements in care and management of livestock or in breeding in the agricultural sector, but should be used in such fields as required.

No.1 Definitions

In these Guidelines, the terms are defined as follows.

1) Animal experiment, etc.

Utilization of animals for education, testing, research, manufacture of biological products or other scientific purposes

2) Facilities, etc.

Facilities and equipment used to perform animal experiments, etc.

3) Laboratory animal

Animal of mammalian, avian or reptilian species used in animal experiments, etc.

4) Institution, etc.

Organization (university, institute, independent administrative body, company, etc.) where animal experiments, etc. are performed

5) Director of institution, etc.

Person with overall responsibility in the institution, etc. for proper and safe conduct of the animal experiments, etc. (dean, director of an institution, principal of a school, chairperson of the board of directors, president, head of an institute, etc.)

6) Animal experiment protocol

Protocol drafted beforehand for the conduct of an animal experiment, etc.

7) Researcher(s)

Person(s) performing the animal experiment, etc.

8) Principal investigator

The researcher who is charge of all duties related to the animal experiment protocol

9) Manager

Person in charge of the laboratory animals and facilities, etc. under the director of the institution, etc. (head of the animal experimentation facilities, department head, etc.)

10) Laboratory animal manager

The laboratory animal manager assists the manager and is in charge of management of the laboratory animals 11) Animal technician

Person in charge of care and management of laboratory animals under the laboratory animal manager or researcher

12) Manager, etc.

Director of the institution, etc., manager, laboratory animal manager, researchers and animal technicians

13) Policies, etc.

Fundamental guidelines and basic policies specified by government agencies related to animal experiments, etc. and "Guidelines for Proper Conduct of Animal Experiments" (these Guidelines) specified by the Science Council of Japan.

14) Regulations, etc.

In-house regulations of research institutions specified for the proper conduct of animal experiments and the proper care and management of laboratory animals based on related laws and ordinances and the policies,

No.2 Responsibilities of the director of the institution, etc.

The director of the institution, etc. bears the final responsibility for the conduct of all experiments conducted in his or her institution. The director of the institution, etc. prepares the facilities, etc. considered necessary for proper care and management of the laboratory animals and proper and safe conduct of the animal experiments, etc., appoints the manager and appoints a person with knowledge and experience related

to laboratory animals as the laboratory animal manager. The director of the institution, etc. also provides education for related persons including the researchers and animal technicians with the cooperation of the manager and laboratory animal manager to inform them of the related laws and regulations and policies, etc.

In each institution, etc., in-house regulations including the authority and responsibilities of the director of the institution, etc., standard operating procedures (SOP) for the conduct of animal experiments, proper care and management of laboratory animals and methods of maintenance and management of facilities, etc. should be established based on the policies, etc.

An Institutional Animal Care and Use Committee should be established in each institution. The director of the institution, etc. requests the Institutional Animal Care and Use Committee to review the animal experiment protocols submitted by principal investigators based on scientific rationale and in consideration of animal welfare. The director of the institution, etc. then approves or does not approve the protocol based on the report of the Institutional Animal Care and Use Committee. After completion of the animal experiment, etc., the director of the institution, etc. examines the results obtained and instructs the principle investigator and manager to make improvements based on advice of the Institutional Animal Care and Use Committee.

The director of the institution, etc. retains the animal experiment protocols, results obtained from the animal experiments and the minutes, etc. of the meetings of the Institutional Animal Care and Use Committee; assures transparency of the animal experiments, etc. and publishes the results within a range that does not interfere with research or corporate activities in consideration of protecting private information and research information. The director of the institution, etc. should take the necessary measures to provide education and training to improve the quality of laboratory animal managers, researchers and animal technicians.

No. 3 Institutional Animal Care and Use Committee

The Institutional Animal Care and Use Committee objectively reviews and inspects animal experiments, etc. at an institution, etc., to assure that they are planned and conducted properly. To achieve this, the Institutional Animal Care and Use Committee should be established independently from any organizations involved in administration of the facilities, etc. The role and organization of an Institutional Animal Care and Use Committee are indicated below.

1) Roles of the Institutional Animal Care and Use Committee

Following consultation with the director of the institution, etc., the Institutional Animal Care and Use

Committee reviews from the standpoint of scientific rationale the animal experiment protocol submitted by the principal investigator in consideration of the "Law for the Humane Treatment and Management of Animals" and "Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain" and reports the results of the review to the director of the institution, etc. The Institutional Animal Care and Use Committee also receives the results of implementation of the animal experiment protocol from the director of the institution, etc., and examines the actual conditions at the facilities, etc., as required before reporting back to the director of the institution, etc. and providing advice.

The Institutional Animal Care and Use Committee obtains details of the situation regarding the education and training of laboratory animal managers, researcher(s) and animal technicians, and offers the director of the institution, etc., advice. The Institutional Animal Care and Use Committee may also participate in education and training as required. Items discussed by the Institutional Animal Care and Use Committee are recorded as the meeting minutes that must be maintained and retained. Institutional Animal Care and Use Committee meeting minutes include the items below.

- (1) Day, time and location of meeting
- (2) Names of members who participated in the meeting
- (3) Details of items discussed at the meeting (details of questions from committee members and answers from principal investigators, etc.), and the results of discussions.
- 2) Institutional Animal Care and Use Committee organization

The Institutional Animal Care and Use Committee is composed of members appointed by the director of the institution, etc. To assure that committee members possess the knowledge required to fulfill the role of the Institutional Animal Care and Use Committee, those appointed are researchers conducting animal experiments, etc., laboratory animal specialists and other persons of knowledge and experience.

The number of committee members is decided taking into consideration factors such as the size of the institution, etc., the scope of the research, and the number of animal experiment protocols submitted. A committee member should not participate in the review of an animal experiment protocol for an experiment for which he or she is principal investigator.

No. 4 Animal experiment protocol drafting and experimental procedures

When conducting animal experiments, etc., the significance of the research and the reasons why animal experiments, etc. are required must be explained. Animal

experiments, etc., must be conducted based on scientific rationale. At the same time, they should be conducted in compliance with the internationally accepted 3R principles of animal experimentation as clarified in amendments of the "Law for the Humane Treatment and Management of Animals" (Law No. 68, June 22, 2005), namely Replacement: the application of alternative methods that do not require the use of animals within limits that allow scientific objectives to be achieved, Reduction: the use of as few animals as possible within limits that allow scientific objectives to be achieved, and Refinement: the application of methods that do not distress the animals or subject them to pain within limits required for use. These 3R principles are the ideology behind both animal experimentation and the handling of laboratory animals. Consequently, within the limits required to achieve the objectives of research, they should be taken into consideration and applied appropriately when conducting animal experiments, etc.

1. Drafting of the animal experiment protocol

In accordance with the above principles, the principal investigator should prepare an animal experiment protocol recording the necessary items in the form (2 below), and submit it to the director of the institution, etc., for approval. The director of the institution, etc., requests the Institutional Animal Care and Use Committee to review the protocol content from a more specialized standpoint. The Institutional Animal Care and Use Committee promptly reviews the protocol and immediately reports the results of the review to the director of the institution, etc. The animal experiment, etc., can begin as soon as the principal investigator has received approval from the director of the institution, etc.

The principal investigator conducts the animal experiment, etc., in compliance with the protocol approved by the director of the institution, etc. If changes to the protocol are required that go beyond the approved scope of the experiment, procedures stipulated in the in-house regulations, etc., should be followed. After completion of the experiment, a report to that effect should be submitted to the director of the institution, etc., in compliance with the in-house regulations, etc. If improvements indicated by the director of the institution, etc., are to be implemented, the principal investigator should confer sufficiently with the laboratory animal manager as required.

Below are examples of items that the principal investigator should consider when preparing a protocol, together with details of the animal experiment protocol form.

1) Items requiring consideration when drafting an animal experiment protocol

- * The objective and necessity of the animal experiment, etc.
- * Whether or not repetition of the animal experiment, etc., is unnecessary.
- * Whether an *in vitro* experiment could be conducted or the animal could be replaced by a phylogenetically lower species (use of alternative methods).
- * Whether a change could be made to a less invasive animal experimentation method.
- * The species of laboratory animals used and the genetic and microbiologic quality
- * The number of laboratory animals used.
- * Educational and training experience of the researcher(s) and animal technician.
- * Reasons why special cages and rearing environment are required.
- * The anticipated disorders, symptoms and severity of pain resulting from experimental procedures.
- * Measures to alleviate pain when it is anticipated that the laboratory animal will suffer severe pain.
- * The use of sedatives, analgesics and anesthetics.
- * Whether major surgical procedures should be repeated.
- * Postoperative management methods.
- * Terminal treatment of laboratory animals (method of euthanasia, etc.).
- * Whether the animal experiment, etc., could possibly affect people or the environment. If so, required measures and procedures.
- * Issues concerning the occupational health and safety of the researcher(s) and animal technicians.

Concerning new animal experiments, etc. on as yet unrecognized research subjects, determining the experimental method and number of animals to use may pose problems. In such cases, attempts should be made to prepare a final protocol after conducting preliminary experiments to ascertain possible appropriate methods and number of animals. For protocols that entail unavoidable, severe pain for the animals, the principal investigator should conduct literature searches to determine whether alternative methods are available. If there are no alternative methods, in cases where the relief of pain through the use of measures such as anesthetics and analgesics is thought to be difficult, it is desirable that advice be obtained from a laboratory animal specialist as required. When this is necessary, it should be clearly noted in the protocol.

- 2) Animal experiment protocol form

 It is advisable to prepare the animal experiment protocol form referring to the examples below.
- (1) Principal investigator
 Name
 Affiliation and position
 Contact address
 Animal experiment experience and education and training

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(2) Name(s) of the researcher(s) [name(s) of
subinvestigators]
(3) Research subject
(4) Research objective
(5) Detailed experimental procedure to be used on the
laboratory animals
(6) Term of animal experiment
(7) Type of animal experiment (details of specific
content)
Testing, research
Education and training
Other (enter specific details)
(8) Laboratory animal species, strain, sex, age, etc, and
number of animals used
(9) Animal experiment location
(10) Rearing methods (rearing location, group or
individual rearing, number of animals per cage in the
case of group rearing, food)
(11) Reasons why an animal experiment, etc., is necessary
(specific details)
No alternative method
Sensitivity and precision of alternative methods are
insufficient
Other (reasons: )
(12) Severity of pain animals are anticipated to suffer
due to each of the procedures (refer to pain
classification indicated in the Consensus Recommendation
on Effective Institutional Animal Care and Use Committees
drawn up by the Scientists Center for Animal Welfare
(SCAW), (Laboratory Animal Science. Special Issue: 11-13,
1987)
(13) Pain alleviation methods for laboratory animals
(specific details)
No measures implemented since pain is mild
No particular problems are thought to exist because
restraint and constraint are short term
Anesthetics and analgesic will be used (drug name: )
No pain alleviation method exists that does not prevent
the scientific objective being achieved (reasons: )
Long-term restraint and constraint are unavoidable
(reasons: )
A humane endpoint will be applied (endpoint
determination: )
Other ()
(14) Animal disposal method (specific details)
Overdose of anesthetic
Inhalation of carbon dioxide
Cervical dislocation
Other ()
(15) Disposal of laboratory animal carcasses
(16) Physical, chemical and biological risk factors, use
of genetically engineered animals
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2 Experimental procedures

When conducting animal experiments, etc., pain suffered by the laboratory animals should be reduced as much as possible within limits that allow the scientific objective to be achieved. Since scientific requirements differ for each animal experiment, etc., the principal investigator should describe specific experimental procedures and the anticipated severity of pain in the animal experiment protocol and receive approval from the director of the institution, etc. after review by the Institutional Animal Care and Use Committee.

The principal investigator should retain test reagents, drugs and laboratory equipment appropriately. In particular, the laws and ordinances concerning the storage of controlled substances such as narcotics, poisons and deleterious substances must be observed. When conducting experimental procedures researchers should bear in mind the following points.

- * Acquisition of skills in restraining laboratory animals, administering drugs, obtaining samples and other techniques.
- * Acquisition of skills relating to surgical procedures (prolonged operative procedures such laparotomy, thoracotomy, craniotomy, orthopedic surgery and other procedures should be conducted under the guidance of a specialist with sufficient knowledge and experience of those procedures.)
- * Pain relief procedures for laboratory animals.
- * Observation of experiment discontinuation and completion criteria (humane endpoint).
- * Acquisition of knowledge and skills related to euthanasia procedures.
- 1) Laboratory and laboratory equipment

Laboratories designed for performing experimental procedures on animals and also for analyzing physiological functions should be constructed to prevent animals escaping and to enable easy cleaning and disinfection to prevent contamination by excrement and blood. Clean, hygienic conditions should be maintained at all times, and every effort made to organize the laboratory to assure that even if a laboratory animal escapes, it can be easily recaptured.

Laboratories for surgical procedures (operating rooms) differ in equipment requirements depending on the physical attributes of the study animal, the number of animals, complexity of the surgical procedure, the number and size of devices used and other factors. Experiments using rodents can be conducted in an ordinary laboratory if it is possible to use aseptic techniques to prevent microbial contamination in the surgical field. With large laboratory animals, surgical procedures are often complex, surgery is prolonged and it is conducted by a surgical team. This requires a correspondingly large operating table, inhalation anesthesia devices, surgical lighting, life monitoring devices and other equipment. Support areas such as examination rooms, X-ray rooms and changing rooms in close proximity to operating rooms should also be provided. In particular, when the objective is to conduct an animal experiment, etc., in which the animal

lives for a long period after surgery, preventive measures against contamination should be implemented, the laboratory should be designed to enable easy cleaning after use and an air conditioning system to supply clean air should also be taken into consideration.

When it is necessary to conduct experimental procedures on laboratory animals in an animal rearing room, the influence on other laboratory animals being reared in the same room should be minimized as much as possible. For dogs, cats, monkeys and other animals exhibiting a high degree of emotional behavior, it is particularly important to assure they do not feel any anxiety from sharing the same room.

2) Animal restraint

Physical restraint refers to localized or general restriction of the normal movements of laboratory animals manually or with devices for examinations, sample collection, dosing and treatment. Restraining devices (restrainers, etc.) should be an appropriate size and easy to use, and should cause laboratory animals as little discomfort and injury as possible. When using restraining devices, training of laboratory animals is required to enable them to become accustomed to the devices and researchers. With dogs, cats and monkeys, if they are conditioned for aggressive restraint, their limbs extend outwards and they assume an immobile posture for short experimental procedures in many cases.

Restraint for a prolonged period in a monkey chair or other device should be avoided unless it is essential for achieving the research objective. Light restraint such as a leash for restraining monkeys or other devices that do not interfere with the natural posture of the animal is applicable within the range of experimental purposes. Items that should be considered concerning restraining devices are indicated below.

- * A restraint period only as long as that required to achieve the research objective.
- * Frequent observation of the condition of laboratory animals.
- * Release from the restraining device of laboratory animals suffering from trauma or poor physical condition due to restraint.
- * Restraining devices should not be considered as rearing devices.
- * Restraining devices should not be used as convenient tools for rearing management.

3) Food and drinking water restrictions

Achieving the objective of some research requires food and water restrictions for laboratory animals. Even if it is indispensable to improve reliability and reproducibility of data from animal experiments, etc., the following items should be carefully considered.

- * Even when food and water restrictions are required for experimental reasons, plans should be made so that the animals ingest the minimum amount of food and water required.
- * A scientific rationale is required for the restriction of food and water for research purposes.
- * To monitor the state of dehydration, physiological and behavioral indices should be observed, and body weight and other parameters measured.

4) Surgical procedures

When subjecting laboratory animals to invasive surgical procedures, particular attention should be paid to the following points to alleviate pain as much as possible to within the limits that do not prevent the objective of the research being achieved.

- * As well as aseptic techniques for the surgery itself, postoperative aseptic techniques and postoperative management are important.
- * Antibiotics should be administered in cases where the alimentary tract or other non-sterile site is surgically exposed or where there is the possibility of reduced immune function due to the surgical procedure. However, administration of antibiotics is not an alternative for aseptic techniques.
- * For major surgery (laparotomy, thoracotomy, craniotomy, etc.), aseptic techniques, anesthetic and analgesic procedures, fluid replacement and keeping the animals warm are essential since body cavities are invaded and exposed resulting in substantial physical and physiological injury.
- * For minor surgery (wound suturing, cannulation of a peripheral blood vessel, etc.), the conditions are not as strict as those for major surgery since body cavities are not exposed and there is virtually no physical injury or it rarely occurs. However, equipment must be sterilized and anesthetics should be used appropriately.
- * Highly invasive, major surgery should be conducted under the guidance of a specialist with sufficient knowledge and experience of the techniques involved.
- 5) Analgesic procedures, anesthetics and postoperative management

The alleviation of pain in laboratory animals is important not only from the standpoint of animal welfare but also to assure the reliability and reproducibility of animal experiments, etc.

- * Analgesic procedures should be initiated when symptoms of pain are perceived in a laboratory animal. When an animal feels pain, species-specific behavior includes vocalization, depressed behavior, abnormal expressions or posture and lack of movement.
- * To be able to perceive an abnormality, it is important to understand the behavioral, physiological and biochemical characteristics of that species (or individual) when at rest and at ease.

* To select analgesic and anesthetic methods that do not interfere with the objective of the research, advice should be obtained from a physician, veterinary surgeon, pharmacist or other specialist as required.

The degree of observation of animals required during the postoperative recovery period depends on the animal species and the contents of the surgery. Attention should be focused on environmental temperature control, monitoring of cardiovascular and respiratory function and postoperative pain, with particular attention paid to symptoms of recovery from anesthesia.

- * To deal with unexpected situations, advice should be obtained from a laboratory animal health management specialist.
- * Monitoring items include depth of anesthesia and physiological functions as well as evaluation of clinical symptoms and general condition.
- * Maintaining normal body temperature is effective for preventing cardiovascular and respiratory disorders caused by anesthetics.
- * During the recovery period after anesthesia, laboratory animals should be kept in a clean location at an appropriate temperature and humidity, with their condition monitored frequently.
- * Consideration should be given to parenteral infusions to maintain the water/ electrolyte balance, and to administration of analgesics and other agents for management of the surgical field.

6) Humane endpoint

The humane endpoint refers to the timing of termination of an experiment (in other words, the timing of the application of euthanasia procedures) to release a laboratory animal from severe pain and suffering. It is a term used in contrast to "death" as an endpoint that is used in protocols of animal experiments where the experiment continues until the animal's death.

- * As a rule, euthanasia procedures should be available for termination of animal experiments, etc.
- * At the final stage of an animal experiment, etc., or when analgesics, sedatives or other agents do not provide relief, euthanasia procedures should be performed to release the laboratory animal from pain and suffering (one pain relief method).
- * Indications of when humane endpoint is applicable include food and water intake difficulties, moribund symptoms (self-injurious behavior, abnormal posture, respiratory disorders, vocalization, etc.), abnormal appearance over a prolonged period with no visible indications of recovery (diarrhea, bleeding, soiled genital area, etc.), sudden weight loss (20% or more over several days), and marked increase in tumor size (10% or more of body weight).

- * Reference should be made to pertinent international guidelines for details concerning determination of the humane endpoint.
- * When conducting animal experiments, etc., in which the degree of pain and suffering is high, such as lethal toxicity studies, infection experiments and radiation experiments, the principal investigator should examine setting of the humane point in the planning stage of the animal experiment, etc.

7) Euthanasia procedures

When disposing of laboratory animals on completion of the experiment in accordance with the animal experiment protocol or due to the laboratory animals being subjected to severe pain and suffering during the course of the experiment when anesthetics and analgesics can not be used in the research, the researcher(s) should conduct euthanasia.

Selection of the agent and method used for the euthanasia procedure depends on the animal species and the objective of the experiment. In general, a chemical method (overdose of a barbiturate anesthetic, administration of a non-explosive inhalation anesthetic or carbon dioxide gas) or a physical method (cervical dislocation, decapitation, exsanguination under anesthesia, etc.) is used. However, from the standpoint of animal welfare, the principal investigator should seek the advice and guidance of a laboratory animal specialist as required since there are slight international differences on what are judged to be appropriate methods of euthanasia for laboratory animals.

- * Euthanasia procedures refer to procedures resulting in the rapid loss of consciousness and then death of a laboratory animal not associated with pain or suffering. In addition to Guidelines on Methods of Sacrificing Laboratory Animals (Notice No.40 of the Prime Minister's Office, July 4, 1995), international guidelines should be taken into consideration.
- * Euthanasia should be performed by methods that do not cause distress to other animals in the laboratory. This requires careful attention because until animals lose consciousness they can vocalize and release pheromones.
- * A person who has acquired the skills required for handling a particular animal species should conduct euthanasia procedures, and the death of the animal should always be verified.