

Recent Trends in Animal experimentation in Japan

— On the Revision and Implementation of the Law for the Humane Treatment and Management of Animals —

HIROMI OMOE
Life Science Research Unit

1 Introduction

Animal experimentation has played a very important role in the life sciences, particularly in health science, which is directly concerned with the survival and health of humankind. It goes without saying that the information gleaned from animal experimentation has contributed a great deal to research into fundamentally important human medicine and veterinary medicine, which of course helps to cure and prevent diseases in both humans and animals, and also contributes to education and training in healthcare technology. In Japan in recent years, how best to ensure the safety and hygiene of food and to take measures against the pollution of the natural environment, have become issues of national concern, and animal experimentation has been used effectively to evaluate such things as food additives and pathogens, and the harmful effects of chemicals and other residual substances found in the natural environment.

Last year, the Law for the Humane Treatment and Management of Animals (hereinafter the Amended Law for the Humane Treatment and Management of Animals)^[2] was amended in order to create legislation that gave consideration to the 3R principles^{*1}. These principles represent the fundamental thinking of the international community in terms of the welfare of laboratory animals used in animal experimentation. In preparation for the implementation of this law, on 1st June 2006, government ministries affected

by the changes worked towards both revision of current standards and guidelines, and the establishment of new standards and guidelines.

Ensuring that animal experimentation is carried out according to these 3R principles is a global trend. The recent revision of the Law for the Humane Treatment and Management of Animals in Japan has provided an appropriate opportunity for change in this country; basic guidelines for carrying out animal experimentation were formulated by relevant government ministries (hereinafter Basic Guidelines for Animal experimentation), and independent management systems for each experimental facility are gradually being put in place.

In this article, I have attempted to outline a picture of the legal management systems in place for animal experimentation in Japan from a scientific point of view. This I will compare to the legal situation regarding animal experimentation in Western countries, and will make suggestions as to what is required in order to improve the independent management systems for animal experimentation in Japan. Further, in regards to the appellations used for types of animal and so on, these have, unless otherwise specified, been matched to those used within the Law for the Humane Treatment and Management of Animals.

Concerning to the several names of regulations, standards and committees etc. in this article, I bestowed their suitable names because I could not identify their official English names on websites.

2 The background to, and an outline of, the Law for the Humane Treatment and Management of Animals — in terms of animal experimentation and laboratory animals —

2-1 *The position in law of animal experimentation and laboratory animals*

The Law for the Humane Treatment and Management of Animals not only contains articles relating to the humane treatment of animals, such as the prevention of cruelty to animals and appropriate ways of treating animals, but also outlines regulations for the correct management of animals. The animals covered by this law are considered to be those that come into close contact with humans, and includes domestic animals, animals exhibited in places such as zoos, and farm animals, as well as laboratory animals. Further, one distinction of this law is that the regulations stipulated differ according to the purpose and role of each category of animal, from domestic dogs and cats, to animals in general.

In regard to the legal position of animal experimentation and laboratory animals within this same law, in as far as this law has been prescribed from an animal welfare perspective, the subject of the regulatory management stipulated within is considered to be ‘laboratory animals (and the improvement of the welfare of such)’ and not ‘animal experimentation (the act of utilizing laboratory animals)*².’ As a result, this law functions in such a way as to provide fundamental principles of policy, and does not contain any stipulations which could have any direct effect on the contents and scope of animal experimentation, such as evaluations of the necessity of animal experimentation, or the scientific appropriateness of experimental technique used.

2-2 *Background to the amendment*

The provisions of and amendments to this law were all carried out on the initiative of the lawmakers themselves. The law was enacted

in September 1973, then referred to as the ‘Law concerning the Protection and Control of Animals’ (issued by the then Ministry of Internal Affairs and Communications). The name was subsequently amended in December 1999 to its current appellation (this previous law is hereinafter referred to as the Old Law for the Humane Treatment and Management of Animals). Jurisdiction was transferred to the Ministry of the Environment (hereinafter MOE) in 2001, as part of the reorganization of central government ministries. It was amended further in June 2005 (Amended Law for the Humane Treatment and Management of Animals).

As part of the 1999 amendment, new measures were included that were intended to improve the environment in which pet animals were kept, as a response to both the increasing awareness of the need to treat animals humanely, and also the fact that the abandonment of, and cruelty to, domestic pets was starting to come to the attention of society. However, provisions concerning animal experimentation were excluded from any amendments, with the comment “self-regulation and independent management based on the current standards*³ shall continue to be seen as fundamental.” Other issues had also been left unamended, such as the need to strengthen regulations for businesses dealing with animals; for this reason a review of the law was begun for completion in 2005, approximately 5 years after the introduction of the amended version, and additional rules, designed to put in place measures deemed necessary through examination, and supplementary resolutions intended to combat issues considered unresolved, were put in place^[4,5].

Each political party carried out investigations necessary for the revision of this law, based on the way that the Law for the Humane Treatment and Management of Animals had been stipulated and subsequently amended through the initiation of members. At the same time, in February 2004 the MOE held the ‘1st Investigative Committee on the Nature of Animal Welfare Management,’ which carried out surveys and investigations into how the law was being carried out. On the basis of the results of such investigations, it was

decided in June 2005 that the law should again be put up for amendment through the initiative of the lawmakers.

2-3 The scope of reform

In terms of regulations regarding laboratory animals and animal experimentation, stipulations on both the welfare of laboratory animals and the ethics of animal experimentation were included in Article 41 of the amended law, 'cases in which animals are provided in order to be utilized for a scientific purpose.' In the old law, only 'Refinement' had been included as a mandatory item from among the 3R principles, which set out international thinking on the welfare of laboratory animals. However, the newly amended law includes the other two Rs, 'Replacement' and 'Reduction', as items for consideration. Thus, the law now covers all of the 3R principles.

3 Regulations on animal experimentation in Japan, Canada, the US and Europe

3-1 International regulations on animal experimentation (Table 1)

The laws and regulations regarding the management and administration of animal

experimentation in each country are based on the international principles laid down by the Council for International Organizations of Medical Sciences (CIOMS). These international principles call for the reaffirmation and continued promotion of the 3R principles, as well as setting out guidelines for the evaluation of pain levels suffered by laboratory animals⁴ and the strengthening of the functions of those bodies which examine and review the contents of animal experimentation.

3-2 Regulations in Japan

(1) Administrative regulations

Animal experimentation and laboratory animals are legally defined within Japan (Table 2). Animals used in laboratory testing should be bred, maintained and provided for those various purposes, and regulations apply to all animals used in tests, from small rodents such as mice and rats, through to cats, dogs, monkeys and birds. In accordance with the advancements in animal biotechnologies⁵ seen in recent years, there have been cases in which domestic livestock, such as pigs and cows, have been used in experimentation¹⁰.

The ethics and principles behind the administrative structure for animal

Table 1 : Outline of the main international guidelines on animal experimentation and laboratory animals

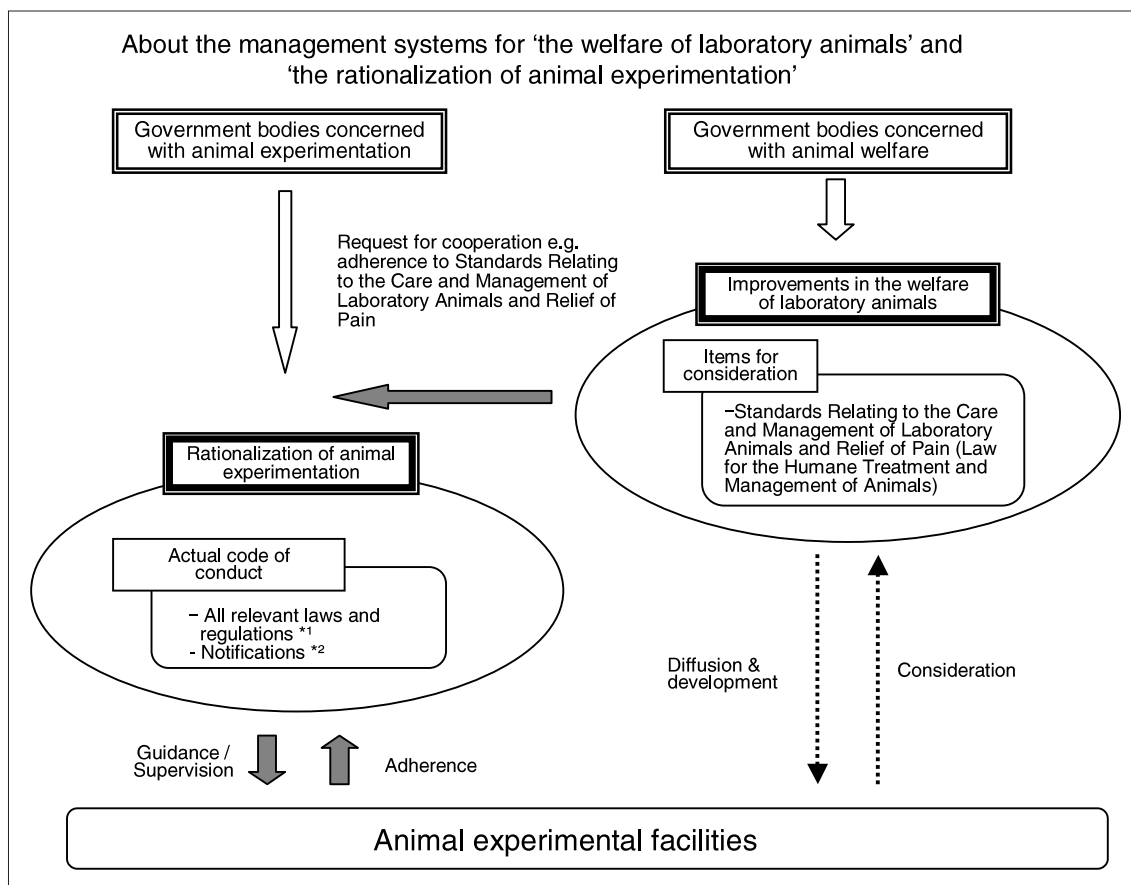
Name of guidelines (Year of enactments / date of newest amendment)	Prescribing body	Outline of guidelines
World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (1964/2004) ⁶	18th World Medical Association (WMA) General Assembly	<ul style="list-style-type: none"> Advocates the ethics and welfare of all humans and animals in biomedical research
Guidelines for the Regulation of Animal Experimentation (1974) ⁷	International Council for Laboratory Animal Science (ICLAS)	<ul style="list-style-type: none"> Forms the basis of current laws and regulations on animal experimentation, prescribes an ethical framework Reinforcement of the concept of the 3Rs Makes clear the responsibility of the head of each facility involved in animal experimentation to ensure that the experimentation carried out is necessary in order to gain improvements in health and healthcare for both humans and animals, and further that objective decision-making is crucial when carrying out animal experimentation
International Guiding Principles for Biomedical Research Involving Animals (1985) ⁸	Council for International Organizations of Medical Sciences (CIOMS)	<ul style="list-style-type: none"> Advocates the promotion and reaffirmation of the significance of the 3R principles Outlines recommendations regarding the scientific and ethical rationalization of legal regulations (e.g. recommendations on the evaluation of pain levels suffered by laboratory animals; the strengthening of the influence of animal experimentation regulatory committees)
Declaration of Bologna: Reduction, Refinement and Replacement Alternatives and Laboratory Animal Procedures (1999) ⁹	3rd World Congress on Alternatives and Animal Use in the Life Sciences	<ul style="list-style-type: none"> Advocates the promotion and reaffirmation of the significance of the 3R principles Outlines recommendations regarding the scientific and ethical rationalization of legal regulations (e.g. recommendations on the evaluation of pain levels suffered by laboratory animals; the strengthening of the influence of animal experimentation regulatory committees)

Prepared by the STFC

Table 2 : Definitions of animal experimentation and laboratory animals

	Laws and regulations	Scope of definition	Intended targets
Animal experimentation	Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain (April 2006, MOE, Notification No. 88)	Provision of animals for the purposes of education, experimental research, and the manufacturing of biologics, and for any other scientific purpose	Education, experimental research, manufacturing of biological drug products and any other scientific purpose
Laboratory animals		Animals which are raised or maintained within facilities in order to be used for experimental purposes (including animals being transported to facilities for those purposes)	Mammals, birds and reptiles

Prepared by the STFC



*1 Pharmaceutical Affairs Law, Industrial Safety and Health Law, Law concerning the Evaluation of Chemical Substances and Regulation of their Manufacture, etc.

*2 Notifications sent by MEXT to all heads of national, public and private universities, etc.

Note: Facilities engaged in the production and reproduction of laboratory animals (Agriculture, Forestry and Fisheries government administration) have been omitted from this chart.

Extracted from Reference^[11]

Figure 1 : Management system for animal experimentation in Japan

experimentation in Japan, as mentioned in Section 2-1, are stipulated in law (Law for the Humane Treatment and Management of Animals), and according to both the proclamation which specifies those regulations that refer specifically to 'animals' (Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain) and the notification on 'experimentation' (regarding Animal Experiments in Universities

etc.), each experimental facility is required to implement a system whereby it is responsible for regulating animal experimentation independently (Figure 1)^[11]. Further, in cases where animal experimentation is carried out for any kind of hazard assessment testing, the scope of any relevant conduct will be bound by the laws and regulations set out in the Pharmaceutical Affairs Law, the Industrial Safety and Health Law, and

Table 3 : Main efforts regarding independent management of animal experimentation in Japan

Government Measures	Measures Taken by the Science Council of Japan and Japanese Association of Laboratory Animal Facilities of National Universities	Measures Taken by Associated Academic Bodies & Associations
<ul style="list-style-type: none"> • Law for the Humane Treatment and Management of Animals (1973 Legislation No. 105; partially amended July, December 1999, partially amended 2005). • Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain (April 2006, MOE, Notification No. 88) • Guidelines on the Disposal of Animals (Prime Minister's Office, Notification No.40, July 1995; partially amended December 2000) • Animal Experiments in Universities etc. (Notification of the Director-General of the Science and International Affairs Bureau, Ministry of Education, Science, Sports and Culture; 1987) (Ministry of Education, Science, Sports and Culture, Information Publication No. 141) • Introduction of Laboratory Animals in Universities etc. (Notification of the Director-General of the Research Promotion Bureau, Ministry of Education, Culture, Sports, Science and Technology (MEXT); January 2001) (12th MEXT Promotional Proclamation No. 42) 	<p>【Science Council of Japan】</p> <ul style="list-style-type: none"> • Planning with Respect to the Guidelines for the Care and Use of Animals (Recommendations) (1980) • Ethical and Practical Problems Encountered During the Treatment of Animals in Education and Research, and Some Suggestions (August 1997), 16th Special Committee on the Relationship between the Development of Life Sciences and Social Understanding • Suggestions on How to Improve Social Understanding of Animal Experimentation (Report No.7, July 2004) <p>【Japanese Association of Laboratory Animal Facilities of National Universities】</p> <ul style="list-style-type: none"> • Guidelines on the Giving and Receiving of Laboratory Animals: Mice and Rats Edition (Final revision, May 2001) • Understanding the Classification of Levels Based on Pain, Distress and Stress Suffered by Laboratory Animals (June 2004) • Basic Concept on the Treatment and Handling of Genetically Modified Animals etc (May 2005) 	<p>【Japanese Association for Laboratory Animal Science】</p> <ul style="list-style-type: none"> • Guidelines on Animal Experimentation <p>【Physiological Society of Japan】</p> <ul style="list-style-type: none"> • Guiding Principles for the Care and Use of Animals in the Field of Physiological Sciences <p>【Japanese Pharmacological Society】</p> <ul style="list-style-type: none"> • Guiding Principles for the Care and Use of Laboratory Animals, Approved by Japanese Pharmacological Society <p>【Japan Neuroscience Society】</p> <ul style="list-style-type: none"> • Guidelines on Animal experimentation within the Japan Neuroscience Society <p>【Japanese Society of Toxicology】</p> <ul style="list-style-type: none"> • Japanese Society of Toxicological Sciences Guidelines on Animal Experimentation <p>【Japanese Society for Laboratory Animal Resources】</p> <ul style="list-style-type: none"> • Laboratory Animal Welfare Charter • Guidelines on the Transportation of Laboratory Animals • Guidelines on the Euthanasia of Laboratory Animals

Prepared by the STFC

Law concerning the Evaluation of Chemical Substances and Regulation of their Manufacture, etc., as well as the Agricultural Chemicals Regulation Law. Depending on the purpose of the experimentation, experimentation may be subject to several laws; no guidelines have been drawn up on creating an integrated method for managing animal experimentation through combining these pieces of legislation into a single comprehensive law.

According to the scope of conduct based on the government guidelines laid out in the above proclamations and notifications, and other relevant legislation, each testing facility must establish a system of independent management and administration; it must set out internal regulations, establish an animal experimentation committee which will be responsible for the review and approval of experimental design, and carry out training programs for those staff responsible for conducting animal experimentation. These internal regulations must

indicate clearly the way in which laboratory animals are to be handled, with a view to their welfare, as well as those scientific methods of use which are acceptable within the facility. The regulations should be drawn up with consideration to the guidelines on animal experimentation that have been published by the Science Council of Japan, the Japanese Association for Laboratory Animal Science (JALAS), the Japanese Society for Laboratory Animal Resources (JSLA), and other academic bodies concerned with animal experimentation (Table 3).

(2) Systems of accreditation through related organizations

In Japan, there is no legal system for the licensing of those persons who carry out animal experimentation. However, JSLA and the Japanese Association for Laboratory Animal Medicine (JALAM), affiliated with the Japanese Society of Veterinary Science (JSVS), has set out guidelines

on skills and technical standards required when handling laboratory animals. Both of these bodies accredit those persons proven to have met these standards by passing an examination: the former confers the Laboratory Animal Technician Diploma (approved by JSLA) and the latter the JALAM-approved Laboratory Animal Veterinarian.

3-3 *Regulations in Europe, the US and Canada*

One feature characteristic of the regulations of animal experimentation in Western countries is that in many cases there are in place legal and regulatory measures, in one form or another, which refer specifically to both the execution of animal experimentation, and to the humane treatment of laboratory animals. The nature of these regulations differs according to country, but one can broadly place them in one of two general categories: the management systems of the United States and Canada, which are centered on the principle that the experimenter themselves will be responsible for individual and autonomous management; and the systems seen in Europe, which tend to place emphasis on management being achieved through regulations overseen by governmental authorities. However, one important similarity is maintained throughout: be it the United States, Canada, or Europe, nationally uniform regulations are in place which are designed to guarantee certain standards for animal experimentation. The responsibility for drawing up these standards differs from country to country. In the United States and Canada, that responsibility lies with organizations concerned with the furthering of scientific research, namely a subsidiary organization of the National Academy of Sciences and a government-controlled NPO respectively, whilst in EU countries, national laws tend to reflect the stipulations of EU Directives.

(1) EU countries

Each member country has established laws relating to animal experimentation according to the following EU Directives: the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other

Scientific Purposes^[12], and the Protection of Animals Used for Experimental and Other Scientific Purposes (EU Directive 86/609/EEC)^[13]. With regard to the latter directive, EU member countries are required to institute this as domestic legislation; this in turn stipulates that countries must establish a system whereby the experimental facilities, the experimental design, and the persons responsible for carrying out the testing must be reviewed and approved directly by the national authorities. Therefore, if those experimental designs, intended to be carried out at facilities deemed to be meeting specific standards as set by the national government, and which are recognized as constituting a balance between both scientific and animal welfare perspectives, are not carried out by a person possessing the appropriate license, then that practice will be punishable as an illegal act.

- United Kingdom

Has a centralized system of laws and regulations in force, based on the Animals Act of 1986[14]. The Home Office oversees a system of certification for animal experimental facilities, for experimental design, and for those who carry out such experiments, based on these laws.

- France

Based on the government ordinance on animal experimentation (No. 87-848), the *Decret aux Expériences Pratiquées sur les Animaux*^[15], a system of accreditation for animal experimental facilities and for persons conducting such experimentation, is in place. However, there are no regulations in place regarding experimental design. The reason for this lies in the fact that reasonable and acceptable experimentation can be achieved through the implementation of thorough education and training, such as training programs for each individual involved in experimentation.

- Germany

An administrative system is in place, based on the Animal Welfare Act^[16]. Accreditation for

animal experimentation is carried out by each state authority, and is carried out for animal experimental facilities, experimental design, and the persons who conduct the experimentation, identical to the UK system. Further, each facility carrying out animal experimentation must appoint an Animal Welfare Officer, who is responsible for procedures relating to the review of experimental design.

(2) Switzerland

Regulations on animal welfare and protection are extant within the constitution, and the Animal Welfare Act of 1978, as well as the Animal Protection Orders of 1981 and 1991, have been set in place on the basis of these. Further, several legally binding guidelines are extant^[17]. The responsibility for implementing these regulations is delegated to each municipal authority, and the relevant body carries out accreditation for animal experimental facilities, experimental design, and the persons who carry out the testing.

(3) United States

Animal experimentation is carried out according to the Animal Welfare Regulations, which are themselves based on the stipulations in the Animal Welfare Act^[18]. Furthermore, nationally uniform guidelines (Guide for the Care and Use of Laboratory Animals, hereafter ILAR Guidelines)^[19] have been issued by the Institute for Laboratory Animal Research (ILAR), which is a subsidiary organization of the National Academy of Sciences. Laboratories are required to carry out experimentation according to these guidelines. In the case of research projects receiving funding from the National Institutes of Health (NIH), experiments are required to adhere strictly to the Public Health Service Policy on Humane Care and Use of Laboratory Animals^[20]. Each animal experimental facility manages itself independently, according to the above regulations. However, the Association for Assessment and Accreditation of Laboratory

Animal Care (AAALAC), a third party independent body, is responsible for investigating whether or not animal experimentation is being carried out appropriately. There is no program of accreditation for experimental design, nor for animal experimenter, but research institutes are required to set up an Institutional Animal Care and Use Committee (IACUC), which reviews and approves experimental design plans.

(4) Canada

Although there are no laws relating specifically to animal experimentation, nationally uniform guidelines^[21], which stipulate specific standards of management, are in place. The Canadian Council on Animal Care (CCAC), a government-controlled NPO, plays a central role in the management system, and is responsible for carrying out inspections of animal experimental facilities, among other duties. In the same way as the US, Canada requires laboratories to establish bodies that are responsible for the review and approval of experimental design plans; in Canada, such bodies are referred to as Animal Care Committees (ACC).

3-4 *A comparison of the regulatory systems of Japan, Canada, the US and Europe*

Table 4 represents a comparison of the management systems in place for animal experimentation within Japan, with those of the European nations, the United States and Canada.

In the sense that the management system in Japan also centers on the concept of self-regulation and individual management for animal experimentation, it is similar to those found in the United States and Canada. In the US, as well as implementing an independent management system, testing laboratories are required to notify and report to designated bodies, to undergo inspections by the government, and to implement the nationally uniform guidelines stipulated.

Table 4 : Comparison between the management systems in place for animal experimentation within Japan, and those in Europe, the US and Canada

Country	Name of law, date of implementation, date of newest amendment	Regulatory body	Animals affected	Accrediting body for: experimenter / facility / experimental design	Inspections / Investigatory visits	Committees on animal testing	Guidelines & Standards
Japan	Law for the Humane Treatment and Management of Animals 1999/2005 (Law concerning the Protection and Control of Animals was enacted in 1973)	MOE	<ul style="list-style-type: none"> Differs according to the measures and regulations in place, from those specific to dogs & cats, to those covering all animals in general animals under humane treatment: mammals, birds and reptiles which have an especially close relationship with humans 	None / None / Internal committees within experimental facilities	None	<ul style="list-style-type: none"> Internal committees within experimental facilities 	<ul style="list-style-type: none"> Legal guidelines on the care and management of laboratory animals Internal standards for each experimental facility (After June 2006, standards set by relevant government ministries should come into effect)
United States	Animal Welfare Act 1970/1985	Department of Agriculture	All warm-blooded animals (excluding mice, rats and birds)	None / Secretary of the Department of Agriculture / Internal committees within experimental facilities	Department of Agriculture-affiliated investigating officer	<ul style="list-style-type: none"> Internal committees within experimental facilities: Institutional Animal Care and Use Committees (IACUC), responsible for experimental design review etc. 	<ul style="list-style-type: none"> Uniform guidelines set by the Institute for Laboratory Animal Research (ILAR) Internal standards for each experimental facility
	Public Health Service Policy on Humane Care and Use of Laboratory Animals 2002	National Institutes of Health (NIH)	* laboratory animals used in research receiving funding from the NIH	None / Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) or the NIH / Internal committees within experimental facilities	Inspections carried out in some specific cases	<ul style="list-style-type: none"> Internal committees within experimental facilities: IACUC (Institutional Animal Care and Use Committees), responsible for experimental design review etc. 	
Canada	Guide to the Care and Use of Experimental Animals	Canadian Council on Animal Care (CCAC)	Living vertebrates, living cephalopods (octopus, squid)	CCAC / CCAC / Internal committees within experimental facilities	CCAC	<ul style="list-style-type: none"> Internal committees within experimental facilities (Animal Care Committees: ACCs) 	<ul style="list-style-type: none"> Uniform standards stipulated by the CCAC Internal standards for each experimental facility
UK	Animals (Scientific Procedures) Act 1986	Home Office	Living vertebrates	Secretary of State / Secretary of State / Secretary of State	Home Office investigating officer	<ul style="list-style-type: none"> National committee: Animal treatment committee, responsible for national policy decisions Internal committees within experimental facilities; ERPs: Ethical Review Process, responsible for experimental design review etc. 	<ul style="list-style-type: none"> Investigatory standards as defined by law
France	Decret aux Expé rience Pratiquées sur les Animaux (No. 87-848) 1987)	Ministry of Agriculture	Living vertebrates	Minister of Agriculture / Minister of Agriculture / None	Facility employees as directed by the Minister of Agriculture	<ul style="list-style-type: none"> No committees at present Currently in the process of setting up a national committee (national committee on laboratory animal ethics) 	<ul style="list-style-type: none"> Investigatory standards as defined by law
Germany	Animal Welfare Act (Experimental Animals Section V) 1972/1998	State government	Vertebrates	State government / State government / State government	State government	<ul style="list-style-type: none"> State committee (no internal committees within experimental facilities) 	<ul style="list-style-type: none"> Investigatory standards as defined by law
Switzer-land	Federal Act on Animal Protection 1978	National government	Vertebrates	State government / State government / State government	State government	<ul style="list-style-type: none"> State committee 	<ul style="list-style-type: none"> Various legally binding standards

Prepared by the STFC based on References^[22,23]

4 Numbers of laboratory animals used in Japan, Canada, the US and Europe

Understanding the numbers of laboratory animals used helps to further an understanding of the current global situation regarding animal experimentation. In this chapter, I have attempted to outline the numbers of laboratory

animals used in experimentation in Japan, and in the European nations, the United States and Canada.

I have also attempted to make comparisons regarding projected changes in the number and type of laboratory animals used in experimentation in Japan and Western countries. However, as previously mentioned, the fact that the systems of management that regulate animal experimentation used are different, differences

Table 5 : Numbers of laboratory animals used in Europe, the United States and Canada

Year of Survey		United States		Canada		United Kingdom	
		2000 ^[26]	2004 ^[26]	1999 ^[27]	2002 ^[28]	2000 ^[27]	2004 ^[24]
Type of animal	Mice	Not subject to Animal Welfare Act		648,550	759,790	1,606,962	1,910,110
	Rats	Not subject to Animal Welfare Act		268,583	332,065	534,973	456,981
	Dogs	69,516	64,932	7,444	9,518	7,635	5,570
	Cats	25,560	23,640	2,576	3,561	1,813	498
	Monkeys	57,518	54,998	1,131	2,109	1,494	2,792
	Other*	1,133,818	958,388	818,322	996,092	561,849	402,678
Total		1,286,412	1,101,958	1,746,606	2,103,135	2,714,726	2,778,629

* Includes rabbits, guinea pigs, hamsters, domestic livestock, birds, amphibians, reptiles and fish

* Classification of animal types used is identical to the references materials used

Prepared by the STFC based on References^[24-28]

are also seen in the methods used to calculate numbers of laboratory animals.

4-1 Numbers of laboratory animals used in Japan

In Japan, there is no law requiring laboratories to make reports regarding the numbers of laboratory animals used in experimentation. However, JALAS conducts research into the number of animals used for such experimentation, and JSLA carries out investigations into the total number of laboratory animals sold within Japan. However, both of these bodies rely on voluntary questionnaires as the basis of their research, and therefore cannot be considered to accurately reflect the actual number of laboratory animals involved in experimentation.

4-2 Numbers of laboratory animals used in the Europe, the US and Canada

Out of those countries which, as a result of legal requirements, both carry out and publish the results of research into the numbers of laboratory animals used in experimentation for the purposes of education, research and safety trials, I have investigated the United States, Canada and the United Kingdom (Table 5).

In terms of general trends, the number of laboratory animals used in each country seems to have either leveled off, or is increasing in only very slightly. In the United Kingdom and Canada, the number of genetically modified mice used is rising, and this is likely to account for the increase in overall figures^[24].

In terms of the type of animal used, mice and rats account for over 50% of the total in both the United Kingdom and Canada, and in terms of total usage represent about 85% in the United Kingdom, and about 52% in Canada, according to the latest data. In the United States, experimentation on mice and rats is not subject to Animal Welfare Act, and therefore the numbers of these animals used in experimentation are not known. However, the National Association for Biomedical Research (NABR) has estimated that experimentation on mice and rats accounts for 85%-90% of the total number of laboratory animals used in the United State^[25].

5 National and international trends in animal experimentation in recent years

5-1 National trends

(1) Stipulations and amendments in guidelines and standards in animal experimentation, and regarding laboratory animals

In response to the clear specifications regarding the 3R principles set out in the Amended Law for the Humane Treatment and Management of Animals, guidelines and standards for concerned government agencies regarding animal experimentation and laboratory animals were formulated and amended. At the Ministry of the Environment, basic standards were altered in order to ensure that methods which minimize the suffering of laboratory animals are used, both in terms of the care and housing

Table 6 : Standards relating to animal experimentation to be notified or communicated in accordance with the implementation of the Amended Law for the Humane Treatment and Management of Animals

Name of legislation, date of implementation	Department responsible	Facilities / institutions affected	Animals affected	Contents
Standards relating to the care and management of laboratory animals and relief pain ^[2] (April 2006, MOE, Notification No. 88)	Subcommittee on Laboratory Animals, Animal Protection Committee, Central Environment Council, MOE	Persons and bodies connected with laboratory animals as follows: <ul style="list-style-type: none"> Managers (those persons responsible for laboratory animals and experimental facilities) Persons responsible for laboratory animals Persons who carry out experimentation Persons who raise and care for laboratory animals Facilities which produce animals for the purposes of laboratory experimentation 	<ul style="list-style-type: none"> Animals being taken care of, or managed in, facilities for the purposes of being used in experimentation Animals being transported to facilities Mammals, birds, reptiles * Excludes animals kept for stockbreeding purposes 	<ul style="list-style-type: none"> Revised 'Standards Relating to the Care and Management of Laboratory Animals' (Notification No. 6, Prime Minister's Office, March 1980) Common standards: health of animals, maintenance of safety standards, maintenance of living conditions and environment, prevention of harm, hazards etc., rationalization of record keeping, appropriation of knowledge about 'Zoonoses', treatment and handling of animals during transportation, treatment and handling of animals when facilities are closed down etc. Individual standards: points for consideration in terms of the actual execution of animal experimentation; points for consideration in terms of the production and provision of laboratory animals
Basic guidelines on animal experimentation in research institutes ^[29] (Notification, June 2006)	Special Committee on Examination of Guidelines on Animal Experimentation, Life Sciences Committee, Subdivision on R&D Planning and Evaluation, Council for Science and Technology, MEXT	Research facilities under the authority of MEXT: <ul style="list-style-type: none"> Universities Universities using joint facilities Specialized vocational high school Facilities under MEXT control Independent administrative institutes under MEXT control Corporations under MEXT control which were established according to Article No.34 of the Civil Law 	<ul style="list-style-type: none"> Animals being taken care of, or managed in, facilities for the purposes of being used in experimentation Mammals, birds, reptiles 	<ul style="list-style-type: none"> Clear indication of the accountable entity: the director of each facility The following should be carried out by each separate facility or institution: <ul style="list-style-type: none"> Drawing up of internal regulations Establishment of an animal research committee Implementation of training and education programs Self checks and evaluation * According to MEXT guidelines, facilities should, as well as implementing a system of self-checking and evaluation, also work to examine the results of any such evaluations Information disclosure
Basic guidelines on the implementation of animal experimentation in facilities under the control of MHLW ^[30] (Notification, June 2006)	Science and Technology Committee, Health Sciences Council, MHLW	The following facilities which carry out animal experimentation (including laboratories affiliated to facilities which carry out animal experimentation) <ul style="list-style-type: none"> Facilities & institutions under the control of MHLW Independent administrative institutes, public interest corporations (under the control of MHLW) Privately-owned corporations (under the control of MHLW that were established according to Article No. 34 of the Civil Law, Law No.89, 1896) Any other corporations under the control of MHLW 	<ul style="list-style-type: none"> Mammals, birds and reptiles being taken care of, or managed in, facilities for the purposes of being used in experimentation 	<ul style="list-style-type: none"> Information disclosure
Under consideration *	Science Council of Japan	Under consideration	Under consideration	Guidelines on animal experimentation that are relevant in terms of the internal regulations drawn up for each experimental facility

* The guidelines were published in June 2006 ('Guidelines on the appropriate implementation on animal experimentation').

Prepared by the STFC based on References^[2,29,30]

of such animals, and their use in scientific experimentation. Furthermore, the Ministry of Education, Culture, Sports, Science and Technology (hereinafter MEXT), and the Ministry of Health, Labour and Welfare (hereinafter MHLW) formulated basic guidelines, to which supervisory organizations will be subject, that were designed to ensure the implementation of a system of animal experimentation that maintains a balance between both science and issues of animal welfare (Table 6)^[2,29,30]. These guidelines and standards set out the fundamental thinking regarding animal experimentation and the management of laboratory animals in Japan, and are not legally enforceable.

The Basic Guidelines for Animal experimentation, as formulated by MEXT and MHLW, set out

those fundamental concepts to be followed when any and all experimentation is carried out. When experimentation is carried out, the necessity arises to stipulate internal regulations for the maintenance and management of experimental facilities, and concrete rules on experimental methodology within relevant institutions. According to the guidelines set out by both ministries, such internal regulations will be formulated for each institution, with consideration to the guidelines set out by the Science Council of Japan.

(2) Research organizations involved in alternatives to animal experimentation
 'Alternatives to animal experimentation' refers to the process of substituting methods

Table 7 : Main research subject for developing alternatives to animal experimentation

Acute toxicity test (reduction in number of animals used, cytotoxic effect test)
Conjunctival irritation test (cytotoxic effect test, protein metamorphic test etc.)
Primary skin irritation test (cytotoxic effect test, 3-dimensional cultured skin model)
Skin permeability test (isolated skin method)
Phototoxicity test (cytotoxic effect test, covalent binding test, histidine oxidization method)
Skin sensitization testing (protein binding test, cultured human skin cell method, cultured Langerhans cell test, skin permeability test, local lymph node assay)
Mutagenicity test
Carcinogenicity test (short-term test*, cell mutagenicity test, peroxisome proliferation test)
Reproductive toxicity test (embryo cultured test, limb bud cell culture test)

The items in bold type are proving particularly active in the development of in vitro alternative methods

* Evaluation test for promoter levels using p53 (tumor suppressor gene) knock-out mice and partially-hepatectomized mice

Extracted from Reference^[31]

of experimentation that use laboratory animals for experimentation that do not. It also covers the reduction of the numbers of laboratory animals used, as well as a relief of pain of laboratory animals used in experimentation. The relevant experimental methods are considered to be essential procedures in the carrying out of animal experimentation based on the 3R principles, and diverse research projects are in place (Table 7). Through the development and subsequent validation^{*6} of new experimental methods based on such research, investigations are being conducted on a global scale to ascertain whether or not such methods could be used in government testing (e.g. the screening of chemical substances).

In Japan, the Japanese Society for Alternatives to Animal Experiments (JSAAE) has for several years played a pivotal role in the development of research into methods that provide alternatives to animal experimentation, and in November 2005, the Japanese Center for the Validation of Alternative Methods (JaCVAM) was established within the Biological Safety Research Center, part of the National Institute of Health Sciences, as a focal point for such research. Accordingly, hopes are high for the continued development of such research into alternatives to animal experimentation.

**(3) Formulation of a system for the systematic collection, preservation and provision of laboratory animals:
the National BioResource Project**

This project was begun in July 2002, as part

of the ‘Research Revolution 2002 (RR2002)’ project overseen by MEXT. Under this project, a structure is being implemented that will allow the systematic collection, preservation and provision of those bioresources (laboratory animals and plants, various cells, the genetic stock of various living organisms etc.) that Japan should be proactively looking to have amassed to international levels by the target year of 2010. As of 1st May 2006, there were 24 types of bioresources in total^[32].

Laboratory animals are also being systematically collected and kept under this project. It is believed that if the systematic breeding, maintenance and usage of laboratory animals become possible, then this will lead both to further rationalization of animal experimentation, as well as improvements in the welfare of laboratory animals.

(4) Establishment of new regulations regarding the areas used to keep genetically modified animals

Research and development on genetically modified animals in Japan is carried out in strict accordance with the following laws and regulations: the domestic law for the implementation of the Cartagena Protocol on Biosafety^{*7}, implemented in February 2004 and known as the Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Law No. 97 of 2003; hereinafter referred to as the Cartagena Law), the Ministerial Ordinance Stipulating those Measures

to be Taken to Prevent Diffusion during the Type 2 Use of Living Modified Organisms on Research and Development (January 2004, MEXT and MOE Ordinance No. 1; hereafter Type 2 R&D Ordinance)*⁸, and the Notice on Ordinances on Research and Development (Amended February 2006, MEXT)^[33,34].

In the Type 2 R&D Ordinance, those measures required to prevent diffusion during animal experimentation are specified, and new regulations are laid out regarding provisions for 'Special breeding section' (enclosed areas, e.g. by fencing), which are not to be closed off. The ability to provide such section is however dependent on the fulfillment of certain conditions specified in the ordinance, such as being able to prove that the recombinant nucleic acids within the genetically modified animals have already been identified, and that any such identified nucleic acids are not related to the pathogenicity. In those cases where conditions are met and such section can be created, then, after ensuring complete installation of two-fold escape control facilities, and a system to identify individual animals, keeping laboratory animals outdoors in an environment closer to that of their natural habitat becomes possible, even if that section remains confined to a certain extent.

Before the implementation of the Cartagena Law, genetically modified animals were kept

under containment, regardless of size, and there were issue of animal welfare, such as the fact that it was not possible to provide larger animals with areas to exercise. Although the scope of application of the regulations concerning these 'Special breeding section' is limited, the fact that such regulations have been established does point to a greater awareness of animal welfare.

5-2 Trends in the Europe, the US and Canada

Regarding the hazard assessment of chemical substances, alternatives to animal experimentation are being actively adopted, and efforts are being made to reduce the number of animal experimentation. At the same time, in the United Kingdom, laws have been established to protect those persons holding licenses allowing them to carry out animal experimentation, as well as animal experimental facilities, from acts of violence and protest; as such, the movement to protect and maintain animal experimentation has grown in strength.

(1) Establishment of regulations to limit animal experimentation

An EU Directive banning safety assessment experiments for cosmetics which use laboratory animals as subjects, and guidelines on alternatives to animal experimentation are being investigated by each country (Table 8).

Table 8 : Significant legislation on animal experimentation implemented overseas in recent years

Date of legislation	Legislating body	Scope of legislation
December 2001 ^[35]	Organisation for Economic Co-operation and Development (OECD)	Agreement to abolish acute toxicity test procedures aimed at calculating LD50 (Guideline for the testing of chemicals No.401), and adoption of alternative methods (Guidelines for the testing chemicals No.420, 423, 425 which allow for a reduction in the number of animals used) (Abolishment to be executed by December 2002)
July 2002 ^[36]	Germany	Basic law of Federal Republic of Germany (constitution) : proclamation and implementation of amendments to Article 20(a) Introduction of animal welfare legislation
March 2003 ^[37]	EU Council	Proclamation of 7th Amendment to EU Directive 76/768/EEC on cosmetic products Complete abolition of all safety tests using animals by 2009 (or by 2013 for certain specific testing)
May 2004 ^[38]	World Organisation for Animal Health (OIE)	Adoption of guidelines on the basic principles of animal welfare. '5 freedoms' for the welfare of domestic livestock (freedom from hunger, thirst and malnutrition, freedom from physical and thermal discomfort, freedom from pain, injury and disease, freedom to express normal patterns of behavior, freedom from fear and distress), and the clarification of the 3R principles in terms of animal experimentation
July 2005 ^[39]	United Kingdom	Enactment of legislation designed to control animal rights fundamentalists Intended to protect animal experimental facilities and those persons involved in animal experimentation

Prepared by the STFC based on References^[35-39]

Table 9 : OECD test guidelines on the safety evaluation of chemicals

<p>【Acute toxicity test】 TG420 Acute oral toxicity – fixed-dose method (Updated guideline, adopted 20th December 2001) TG423 Acute oral toxicity – acute toxic class method (Updated guideline, adopted 20th December 2001) TG425 Acute oral toxicity – up and down procedure (Updated guideline, adopted 20th December 2001)</p>
<p>【Acute inhalation toxicity test】 TG433 Acute inhalation toxicity – fixed-dose procedure (Draft revised guideline June 2004) TG436 Acute inhalation toxicity – acute toxic class method (Draft new guideline December 2004)</p>
<p>【Acute dermal toxicity test】 TG434 Acute dermal toxicity – fixed-dose procedure (Draft new guideline May 2004)</p>
<p>【Skin sensitization test】 TG429 Skin sensitisation – local lymph node assay (Updated guideline, adopted 24th April 2004)</p>
<p>【Skin corrosivity test】 TG430 In vitro skin corrosion - transcutaneous electrical resistance (TER) method (Original guideline, adopted 13th April 2004) TG431 In vitro skin corrosion - Human skin model test (Original guideline, adopted 13th April 2004) TG435 Membrane barrier test methods for skin corrosion (Draft new guideline May 2004)</p>

TG : Test Guidelines

Prepared by the STFC based on References ^[31, 35]

In order to facilitate the sharing between member countries of the safety test data deemed necessary when handling high production volume chemicals, the Organisation for Economic Co-operation and Development (OECD) is pushing for the drawing up of test guidelines which will standardize the methods of assessment testing used in each member country. Based on the Draft Guidance Document: Recognition, Assessment and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation Studies (October 1998), testing methods which require a 50% lethal dose (LD50) as a barometer for evaluating acute toxicity will be abolished, and methods which use fewer laboratory animals, and which are based on the 3R principles, are to be used instead (Table 9).

(2) Development of alternatives to animal experimentation and expansion of centers for alternative methods

Alternatives to animal experimentation began to be investigated in Western countries at a fairly early point in time, and in the mid 1990s a specialized institute was founded to carry out work relating to research into, and assessment of, such alternatives to animal experimentation. Particularly well known are, in the EU, the European Center for the Validation of Alternative Methods (ECVAM)^[40] and, in the United State, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)^[41]. These institutes are in close contact, and carry out joint validation projects. More recently,

the National Center for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)^[42] was established in 2004 in the United Kingdom, and active efforts are being made on a governmental level to further research into alternatives to animal experimentation.

6 Measures required in order to establish a self-regulation and independent management system for animal experimentation within Japan

The 3R principles have been accepted internationally as expedient by those responsible for the carrying out of animal experimentation, and much effort is being put into furthering research into alternatives to animal experimentation. At the same time, animal experimentation continues to be widely used as an important means of observation and analysis in life sciences. Animal experimentation provides opportunities to analyze and resolve complex biological processes, such as the higher functions of the central nervous system, intercellular crosstalk, and also remains an effective technique for furthering the development of medical technologies. Animal experimentation can also be used successfully in research conducted with a view to establishing treatment and preventative methods for emerging and reemerging infectious diseases so prominent in the news recently, as well as in the evaluation of harmful effects of environmental pollutants. The role of animal

experimentation in cases such as these continues to diversify, and can be expected to continue to do so in the near future.

With the establishment of the Basic Guidelines for Animal experimentation, stipulated after the amendments to the Law for the Humane Treatment and Management of Animals last year, and the creation of standards for the fair management and treatment of laboratory animals, a system of management for animal experimentation and laboratory animals is in the process of being established within Japan. As mentioned in Chapter 3, the management system for animal experimentation in Japan is based around a system of self-regulation and independent management, carried out by each institution and facility performing animal experimentation. The practical regulations for these systems are shouldered by governmental directives, through proclamations and notifications from the relevant governmental bodies, and the code of conduct determined by associated laws and regulations. The standards and guidelines mentioned above should help to further the establishment of a self-regulation and independent management system, and can be considered a milestone in terms of the construction of an original system of management for animal experimentation within Japan.

In order to facilitate the creation of an independent management system for animal experimentation carried out within Japan, certain measures will need to be put in place that can guarantee the Basic Guidelines for Animal experimentation mentioned above. With this in mind, in this chapter I will provide an overview of those measures required in order to ensure the creation of an independent management system for animal experimentation in Japan from now on.

Creation of an evaluating body to oversee facilities carrying out animal experimentation

In the United States and Canada, animal experiment committees are established within those institutes carrying out such experimentation, and are responsible for the review and evaluation of the legitimacy of all animal experimentation. At the same time, third

party bodies also independently evaluate the systems of management in place at those facilities where animal experimentation is being carried out (AAALAC in the United States, CCAC in Canada). Although the process of review for each individual program of animal experimentation in Japan resembles those of the United States and Canada, Japan as yet has no organization responsible for the evaluation of animal experimental facilities.

When a piece of scientific research which involves animal experimentation is submitted for inclusion in an international scientific journal, as well during the scientific review process, the ethical treatment of the laboratory animals used becomes subject to investigation. Should questions arise over the ethics of the submitted report, then it will not be accepted for publication. The fact that, up until now, results from research using laboratory animals carried out in Japan have been published in numerous such international scientific journals, implies that the independent system of management currently in place in Japan is comparable to international standards. However, it remains a fact that there may well exist gaps in the management standards of different experimental facilities. In order to eliminate such potential problems, each experimental facility should be required to adhere to the Basic Guidelines for Animal experimentation stipulated by the relevant governmental bodies. It also goes without saying that experimenters in such facilities must be prepared to make the necessary efforts to ensure that their independent management systems function effectively, and it would seem expedient to establish a system to evaluate experimental facilities. This evaluation system is crucial if Japan is to achieve greater levels of objectivity and transparency within the independent management systems in those facilities.

An evaluation system complete with the functions mentioned above could take on many forms, but here I would like to suggest the creation of a special body with the specific task of carrying out evaluations of experimental facilities involved in animal experimentation. The role of such a body would be to evaluate the internal regulations in place within each

experimental facility, and the conditions under which experimentation is taking place, as well as to provide guidance and instruction as and when necessary. The body would not be responsible for reviewing the content of experimental design plan regarding animal experimentation. Placing the evaluation of proposed animal experimental designs outside the jurisdiction of such a body should be considered from the perspective of protecting intellectual property rights related to research utilizing animal experimentation, and the privacy of assessment testing on toxicity and so forth.

Acknowledgments

I would like to thank Dr. Kazuya Yamanouchi, Professor Emeritus at the University of Tokyo, and Dr. Yasuhiro Yoshikawa, Professor of the Department of Biomedical Science, Veterinary Medical Sciences, Graduate School of Agricultural and Life Sciences of the University of Tokyo, for their invaluable advice and support during the writing of this report.

I would also like to thank Dr. Kazuo Oowada, Councillor of the Safety and Environmental Protection Department, National Institute of Advanced Industrial Science and Technology, for his most helpful comments on the actual state of animal experimentation within Japan today. From Dr. Yukihisa Matsuda, Associate Professor at the Animal Research Laboratory, Bioscience Education-Research Center at Akita University, I received valuable documentation on current animal experimentation practices in various foreign countries. He also kindly engaged in discussions on this report with me, focusing mainly on the legal regulations on animal experimentation extant in both Japan and overseas. Finally, Dr. Shigeru Kyuwa, Associate Professor of the Department of Biomedical Science, Veterinary Medical Sciences, Graduate School of Agricultural and Life Sciences of the University of Tokyo, was also kind enough to share with me his insightful opinions on the welfare of genetically modified animals. I would like to thank everyone who has contributed their time and effort to helping me complete this report.

Glossary

*1 3R

Stands for 'Replacement,' 'Reduction' and 'Refinement.' These three fundamental principles were first advocated in the United Kingdom in 1959 by Russell and Burch as a more humane approach to animal experimentation^[1]. The concept behind the philosophy represented by these principles is to implement the 3Rs within the Law for the Humane Treatment and Management of Animals, wherever possible, and in a way that will not have a detrimental affect on achieving the scientific objectives behind the use of animals in experimentation. 'Replacement' refers to the use, wherever possible, of alternative means of experimentation which do not use animals; 'Reduction' refers to decreasing, wherever possible, the numbers of animals used in experimentation; and 'Refinement' refers to using, wherever possible, methods of experimentation that relieve pain of the animals. In recent years, a fourth R has been occasionally added, meaning either 'Responsibility' or 'Review.'

*2 The welfare of laboratory animals (animal protection) and methods used in animal experimentation

The welfare of laboratory animals (animal protection) and the methods used in animal experimentation are fundamentally considered to be two separate issues. The welfare of laboratory animals is seen to consist mainly of 'the abstract concept of observing the 3R philosophy,' as well as 'practical conduct'; practical conduct can be described as the appropriate implementation of such matters as the care and housing of laboratory animals, the relief of pain during experimentation and the disposal of laboratory animals after the completion of experimentation (including euthanasia). However, the scientific appropriateness of animal experimentation within scientific research, and the guarantee of reproducibility, are required as conditions that must be met for animal experimentation to be considered appropriate. As such,

perspectives on the scope of conduct and the rationalization of said conduct differ⁽³⁾.

*3 Current standards

Refers to the 'Standards Relating to the Care and Management of Laboratory Animals' (March 1980, Proclamation No. 6, Prime Minister's Office; hereinafter Laboratory Animal Care and Management Standards). These were amended and proclaimed in April 2006 (See Chapter 5).

*4 Categories of research experiments based on levels of pain, distress and stress suffered by laboratory animals

A classification system for animal experimentation based on levels of pain, distress and stress suffered by laboratory animals. It was drawn up to act as the basis for making judgments on Refinement issues. Various systems of classification exist, and there is no globally uniform system. Most of the systems used in Japan are based on the classification system developed by the Scientists Center for Animal Welfare (SCAW) in the United States, and the Japanese Association of Laboratory Animal Facilities of National Universities issued a practical guide to standards, called 'Understanding the Classification of Levels Based on Pain, Distress and Stress Suffered by Laboratory Animals' in June 2004.

*5 Animal biotechnologies

This refers to technologies that are used in the manufacturing of pharmaceuticals, and the production of organs intended for xenotransplantation, which utilize genetically modified domestic livestock that have been created through genetic engineering and reproduction technologies. This is a new area that directly connects domestic livestock and medical sciences, and as such is currently attracting a great deal of attention.

*6 Validation

This refers to one of the necessary steps involved in the development of new safety evaluation testing. It demonstrates both the validity and reproducibility of test results, and is a process which is required in order to confirm that the relevant test is indeed

reliable enough to be used in specific toxicity testing.

*7 Cartagena Protocol on Biosafety

This was adopted in January 2000 after the Convention on Biological Diversity made in 1992 at the UN Conference on Environment and Development (also known as the Earth Summit), and is designed to prevent potential ramifications (in terms of the effect on human health) on biological diversity through the use of Living Modified Organisms (LMO). Subject to this convention are such things as genetically modified farm produce and microorganisms; drugs and medicines used for people are not included in the scope of the convention. So far, 132 nations have ratified the convention (as of 1st March 2006).

*8 Regulations on the usage of Living Modified Organisms in the Cartagena Law

According to the Cartagena Law, prior to the use of LMOs, measures need to be put in place according to a system of LMO usage which defines two types of use: Type 1 (use without measures to prevent dispersal into the environment, such as cultivation and importation) and Type 2 (use with measures to prevent dispersal into the environment, required in experimental facilities and factories etc.). Type 2 usage must be accompanied by preventative measures against dispersal, and those preventative measures in place differ for usage within research and development (under the authority of MEXT and MOE) and industrial usage (under the joint authority of the Ministry of Finance, MHLW, the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Economy, Trade and Industry, and the MOE).

Abbreviations

•AAALAC	American Association for the Accreditation of Laboratory Animal Care (USA)
•ACC	Animal Care Committee (Canada)
•CCAC	Canadian Council on Animal Care
•CIOMS	Council for International Organizations of Medical Sciences

- ECVAM* European Center for the Validation of Alternative Methods
- FAWC* Farm Animal Welfare Council
- IACUC* Institutional Animal Care and Use Committees (USA)
- ICCVAM* Interagency Coordinating Committee on the Validation of Alternative Methods (USA)
- ICLAS* International Council for Laboratory Animal Science
- ILAR* Institute for Laboratory Animal Research, Component of the National Research Council, National Academy of Science (USA)
- JaCVAM* Japanese Center for the Validation of alternative Methods
- JALAS* Japanese Association for Laboratory Animal Science
- JSAAE* Japanese Society for Alternative to Animal Experiments
- JSLA* Japanese Society for Laboratory Animal Resource
- JSVS* Japanese Society of Veterinary Science
- NABR* National Association for Biomedical Research (USA)
- NC3Rs* National Center for the Replacemnet, Refinement and Reduction of Animals in Research (UK)
- NIH* National Institutes of Health (USA)

References

[1] Russell, W.M.S. and Burch, R.L. (1959) The Principles of Humane Experimental Technique. London: Methuen. (Web version): http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm

[2] Laws and Regulations on the “Law for the Humane Treatment and Management of Animals”: Nature Conservation Bureau, Ministry of the Environment: http://www.env.go.jp/nature/dobutsu/aigo/law_series/law_index.html

[3] Report 1 from the 6th Annual Investigative Committee on the Nature of Animal Welfare Management (held 4th August 2004): <http://www.env.go.jp/nature/dobutsu/aigo/>

[meeing/pdf/h16_06/mat01.pdf](http://www.env.go.jp/nature/dobutsu/aigo/meeing/pdf/h16_06/mat01.pdf)

[4] Memorandum from the 1st Meeting of the Animal Protection Committee, Central Environment Council, Ministry of the Environment (held 19th March 2001): <http://www.env.go.jp/council/14animal/y140-01a.html>

[5] Report 2 from the 9th Meeting of the Animal Protection Committee on the amendment to the Law for the Humane Treatment and Management of Animals, Central Environment Council, Ministry of the Environment (held 4th August 2005): <http://www.env.go.jp/council/14animal/y140-09/mat02.pdf>

[6] World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects (Helsinki Declaration): <http://www.wma.net/e/policy/pdf/17c.pdf>

[7] ICLAS (International Council for Laboratory Animal Science) Special Reprints. Guidelines for the Regulation of Animal Experimentation. 1974

[8] CIOMS (Council for International Organizations of Medical Sciences) International Guiding Principles for Biomedical Research Involving Animals.: http://www.cioms.ch/frame_1985_texts_of_guidelines.htm

[9] Declaration of Bologna: <http://www.soc.nii.ac.jp/jsaae/bo-e.html>

[10] Kazuya Yamanouchi, “Xenotransplants: the miraculous medicine of the 21st century,” Kawade Shobo Shinsha, 1999 (in Japanese)

[11] Report 7, on those ministerial orders which will need to be put in place relating to management systems, in terms of ‘the welfare of laboratory animals’ and ‘the rationalization of animal experimentation,’ in accordance with the amended law, 9th meeting of the Animal Protection Committee, Central Environment Council, Ministry of the Environment (held on 4th August 2005): <http://www.env.go.jp/council/14animal/y140-09/mat07-2.pdf>

[12] European Convention for the Protection of Vertebrate Animals Use for Experimental

- and Other Scientific Purposes. (European Agreement): <http://www.uku.fi/vkek/Sopimus/convention.html>
- [13] EU Directive 86/609/EEC: http://europa.eu.int/comm/food/fs/aw/aw_1/legislation/scientific/86-609-eeec_en.pdf
- [14] Animals (Scientific procedures) Act 1986 (United Kingdom Animals Act): <http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm>
- [15] France, Decret aux Exp_riences Pratiq_es sur les Animaux, 19th October 1987 (Jikken doubutsu kaigai gijutsu tokushuu No.6): <http://jsla.lin.go.jp/kaigai-sp/sp-kaigai06.html>
- [16] Section V Experiments on Animals (German Animal Welfare Act): <http://www.med.akita-u.ac.jp/~doubutu/regulation/GermanAWA.html>
- [17] Hitoshi Aoki, "The comparative legal culture of animals: A comparison of animal welfare laws in Japan and Europe," Yuhikaku Publishing Co., Ltd., 2002. (in Japanese)
- [18] Animal Welfare Act as Amended (7 USC, 2131-2156) (United States Animal Welfare Act): <http://www.nal.usda.gov/awic/legislat/awa.htm>
- [19] Guide for the Care and Use of Laboratory Animals (1996) (ILAR Standards): <http://www.nap.edu/readingroom/books/labrats/index.html>
- [20] Public Health Service Policy on Humane Care and Use of Laboratory Animals. Office of Laboratory Animal Welfare. Amended August, 2002 (Standards prescribed by the NIH in the United States): <http://grants.nih.gov/grants/olaw/references/phspol.htm>
- [21] List of CCAC Guidelines (Canadian Council on Animal Care Guidelines): http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/GDLINES/Guidelis.htm
- [22] Reference Material 3, Outline of various international animal experimentation regulations, 6th Investigative Committee on the Nature of Animal Welfare Management (held 4th August 2004): http://www.env.go.jp/nature/dobutsu/aigo/meeing/pdf/h16_06/mat01.pdf (in Japanese)
- [23] Yukihiisa Matsuda, "The current state of regulations on animal experimentation in various foreign countries, and the role of animal experimentation committees": <http://www.med.akita-u.ac.jp/~doubutu/jalam/2001/2001.html> (in Japanese)
- [24] Statistics on the Use of Animals, UK Home Office (Number of animals used in testing in the United Kingdom in 2004): <http://www.official-documents.co.uk/document/cm67/6713/6713.pdf>
- [25] National Association for Biomedical Research (NABR): <http://www.nabr.org/>
- [26] Number of Animals Used by Research From the First Reporting Year (FY1973) to the Present, United States Department of Agriculture (Number of laboratory animals used in testing in the United States): <http://www.aphis.usda.gov/ac/awreports/awreport2004.pdf>
- [27] Yukihiisa Matsuda, "Trends in the numbers and kinds of animals used in testing as seen at the 4th World Congress on Alternatives and Animal Use in the Life Sciences": <http://www.med.akita-u.ac.jp/~doubutu/matsuda/kougi/daitaiho.html> (in Japanese)
- [28] Canadian Council on Animal Care. Annual Report 2004-2005 (Number of animals used in testing in Canada): http://www.ccac.ca/en/Publications/PUBLICAT/Annualre/ccac_ar_2004-2005_en.pdf
- [29] "On the proposed basic guidelines on animal experimentation in research laboratories," MEXT Life Science Portal Site, Approaches and efforts being made by commissions and other bodies, Special Committee on Examination of Animal experimentation Guidelines: <http://www.lifescience-mext.jp/policies/shingikai.html> (in Japanese)
- [30] "On the proposed basic guidelines on the carrying out of animal experimentation within the MHLW," 31st Science and Technology Committee, Health Sciences Council, MHLW (held 18th May 2006) (in Japanese)
- [31] Yasuo Ohno, "On the current situation of animal experimentation alternatives," Workshop on animal experimentation methods, Japanese Society for Laboratory

- Animal Resources, 2005 (in Japanese)
- [32] Official website of the National BioResource Project within the MEXT Life Science Portal Site: <http://www.nbrp.jp/index.jsp>
- [33] Homepage for the MEXT governed "Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms":
http://www.mext.go.jp/a_menu/shinkou/seimei/kumikae.htm
- [34] Shigeru Kyuwa, "Effects of the Cartagena Protocol on industrial and laboratory animals," "Transgenic technologies in the fields of laboratory animals and livestock", presented at the Japanese Society for Laboratory Animal Resources, Education Seminar Forum 2006 (in Japanese)
- [35] OECD Chemicals Testing-Guidelines:
http://www.oecd.org/department/0,2688,en_2649_34377_1_1_1_1_1,00.html
- [36] Tadashi Watanabe, "International Laws: Introduction of regulations on animal protection as part of the overall amendment of the basic law in the Federal Republic of Germany" 214 (2002.11):
<http://www.ndl.go.jp/jp/data/publication/le-gis/214/21406.pdf> (in Japanese)
- [37] European Commission (2003) DIRECTIVE 2003/15/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 February 2003, Amending Council Directive 76/768/EEC on the Approximation of the Laws of the Member States Relating to Cosmetic Products, Official J. European Union, L66/26.
- [38] 72nd Annual General Session of the International Committee of the World Organization for Animal Health (OIE):
http://www.oie.int/eng/press/en_040528.htm
- [39] Monday 31 January 2005 10:09 (GNN (Government News Network) News), Hewitt Announces New Law to Crack Down on Animal Rights Experiments (New law in the United Kingdom):
<http://www.gnn.gov.uk/environment/detail.asp?ReleaseID=143791%0D>
- [40] European Center for the Validation of Alternative Methods (ECVAM):
<http://ecvam.jrc.cec.eu.int/index.htm>
- [41] Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM):
<http://iccvam.niehs.nih.gov/>
- [42] National Center for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs):
<http://www.nc3rs.org.uk/>

* All URL addresses correct as of 1st May 2006



Hiromi OMOE, DVM, PhD
Life Science Unit

Veterinarian, Doctor of Philosophy (Agricultural Studies). Took up her current position after participating in molecular pathology research into both human and animal diseases. Interested in policy on scientific technology where it is used to ensure the safety of such things as foodstuffs, microorganisms, and chemical products, which are all factors in daily living.

(Original Japanese version: published in May 2006)