

Education and training system in Japanese research laboratories in a global pharmaceutical company

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Abstract

The Japanese standards relating to the Care and Management of Laboratory Animals and Relief of Pain was revised on June 1, 2006, based on the amendment of the Japanese Law for Humane Treatment and Management of Animals, which added the "3 Rs" principle. To complement the new standards, the Science Council of Japan has published detailed guidelines, titled "Guidelines for Proper Conduct of Animal Experimentation." The guidelines prescribe the roles of the director of Institution, and Institutional Animal Care and Use Committee, as well as the Items of contents in Animal Care and Use Program, Humane Experimental Procedures, and so on. Additionally, they also direct the director of Institution to conduct proper education and/or training for research and care staffs, which are 1) Laws, Standards, Regulations, and so on; 2) Animal experiments and handlings of Laboratory Animals; 3) Care and Management of Laboratory Animals; 4) Safety Management (Environmental Health and Safety); 5) Animal Facilities, and 6) Continuous Education, if necessary. This paper refers to a revised education system according to this guideline for all animal-related staff and continuous education program of animal ethics for all staff in Pfizer Global Research and Development (PGRD), Nagoya Laboratories.

Keywords: long-term education, institutional official, research organization, culture

Introduction

The Law for Care and Management of Animals was established in 1973 (October 1st) in Japan, and it was extensively amended in 1999 and renamed the Law for Humane Treatment and Management of Animals. After this amendment, animals have been recognized as living things, as differentiated from non-living things. As a result, cruel treatment of animals is punished more severely than destruction of property. In addition, animal-related business enterprises, such as pet shops, breeders, horse riding clubs, and so on, are required to be licensed accordingly. The Law, however, did not cover all Laboratory Animals because of the animal health and welfare self-management in breeding and research organizations (Kagiyama N. et al., 2006).

The current Japanese Laws and guidelines concerning animals and/or laboratory animals were presented at WC5, and then two points of consideration were brought up (Suzuki M, 2005). One was a lack of authorized guidelines concerning animal experimentation, and the other was the self-management of animal experiments in each laboratory. Because there are no common guidelines and/or standards in place, most institutions have

their own independent guidelines. It was suggested that the absence of common guidelines is an issue as it concerns the inspection of facilities or animal care and management by a third party for practical implementation. To support this opinion, the Science Council of Japan has released the statement "To promote social understanding to the animal experiment", for the promotion of internal and external understanding of animal experimentation conducted in Japan.

The Law for Humane Treatment and Management of Animals in Japan was amended and the basic principle of animal experimentation – the 3 Rs (Replacement, Reduction, Refinement) – was added, and it was effective on June 1, 2006. In addition to the principle, a provision of the settlement of standards and guidelines for animal experimentation was introduced. This amendment was also effective on June 1, 2006. It had been discussed how to comply with these standards. It was assumed that the standards of animal experiments as a concept are not new, but the standards concerning laboratory animals was revised to include standards relating to the care and management of laboratory animals and relief of pain.

Now, the responsibilities of the director of Institution are clearly described in the standards, and education and training of staff is one of his or her responsibilities, which are essential and indispensable. Here, the amended points of the law concerning animals in Japan will be explained, and the points of revised standards and guidelines which followed it. It also will be explained what kind of educational program is required for institutions containing animal facilities, and how PGRD Nagoya Laboratories adapted their educational programs to them. Then, the necessity of long-term education from the perspective of research systems (High-Throughput Screening System), which have been widely developed in all pharmaceutical research institutions, will be discussed.

Background

1) The Standards for Laboratory Animals

The revised standards for laboratory animals was released from the Ministry of Environment on June 1st, 2006, and renamed to the "Standard for Laboratory Animal Care and Management, and Relief of Pain," in accordance with the addition of the concept of the 3 Rs in the Law for animals. The revised standards comprise General Principles, Definitions, Common Standards, Separate Standards, Application and Exceptions. In the article of common standards, the standards concerning animal care and management are included. For example, methods of animal care and management, construction of animal facilities, education and training, emergency responses, records of laboratory animals, and so on.

In an article of separate standards, the contents consist of two components, animal experiments conducting facilities and laboratory animal breeding facilities, and several considerations in each facility are described here. For conduction of animal experiment in research institutes, they ask us to pay attention to the reduction of pain, suffering and distress of laboratory animals, and the settlement of humane endpoints. They also require conducting proper euthanasia of animals used in experiments.

2) The Guidelines for Animal Experimentation

Although they have been released, neither the Handbook nor guidelines from the Ministry of Environment detailing the Law and standards are yet available. However, The Ministry of Health, Labor and Welfare, the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Agriculture, Forestry and Fisheries have shown each basic guideline as the competent authorities, respectively. The contents of these guidelines are all quite similar, because they originated from the "Guidelines for proper conduct of animal experiments" (<http://www.scj.go.jp/ja/info/kohyo/>

[pdf/kohyo-20-k16-2e.pdf](http://www.scj.go.jp/ja/info/kohyo-20-k16-2e.pdf)) by the Science Council of Japan. The guidelines are outlined in eleven Chapters.

1. Definitions
2. Responsibility of the director of the institution
3. Institutional Animal Care and Use Committee
4. Animal experiment protocol drafting and experimental procedures
5. Laboratory animal selection and receipt
6. Care and management of laboratory animals
7. Laboratory animal health management
8. Facilities
9. Safety Management
10. Education and Training
11. Others.

As with the roles of the director of the institution (such as institutional officials in the U.S.), his or her responsibility is described as: 1) proper care and management of laboratory animals, 2) proper and safe conduct of the animal experiments, 3) appoint a person with knowledge and experience related to laboratory animals as the laboratory animal manager, 4) settlement of in-house guidelines and/or Standard Operating Procedures, and 5) establishment of an institutional animal care and use committee (IACUC), and 6) obtain the results of animal experiments and instruct the principle investigator and manager to make improvements based on advice of the IACUC, for taking the final responsibility for all animal experiments conducted in the institution. The responsibility of the IACUC is described as: 1) review of the animal experiment protocol from the standpoint of scientific rationale, 2) examination of the actual conditions at the facilities, and 3) obtain the detailed education and training records and conduct education and training programs.

The guidelines cover the items concerning animal care and management (delivery, transport, receipt, quarantine and acclimatization of laboratory animals, their caged environment and room environment, retention of records, veterinary care, and so on), and animal experimentation (consideration points of an animal experiment protocol, protocol forms, and the points to bear in mind for the researcher when conducting experimental procedures), similar to the guidelines of ILAR. They also cover the necessity of the settlement of humane endpoints and procedures of euthanasia in animal experiment protocol.

3) Education and training

A one of the roles of the director of the institute, he or she is required to try to provide separate education and training for the Laboratory Animal Manager, Researcher(s) and Animal technicians. The guidelines refer to the timing of education and training, and require the director to provide this

prior to them engaging in animal experiments, and after, as required. They also recommend it should be conducted in accordance with in-house regulations, and the dates of instruction, educational contents, the names of the instructors and those receiving instruction should also be recorded and retained. The contents of education and training should be specified in the in-house regulations taking into account the activities undertaken in the particular institute. Moreover, these items are described to be included in education and training, from the viewpoint of the proper conduct of animal experiments:

- Items related to pertinent laws and ordinances, by-laws, guidelines, and in-house regulations
- Items related to animal experiments, etc., and the handling of laboratory animals
- Items related to the care and management of laboratory animals
- Items related to safety assurance
- Items related to the use of facilities

To answer these requirements, PGRD Nagoya Laboratories have provided new education and training programs. For the educational program related to pertinent laws and ordinances, by-laws, guidelines, and in-house regulations, they have provided a school-like education program that is conducted prior to any handling of laboratory animals and, when it is required, just after the revision of them. This takes into account that the Law is reviewed every five years. For the educational program related to the care and management of laboratory animals, they have provided an education program with their original handbook according to the animal facilities, and have also provided practice-form training programs for each species and/or each procedure. All animal technicians should be authorized by a supervisor who is an expert in each area prior to the handling of an animal or the conducting of a certain procedure. For the educational program related to safety assurance (Zoonosis, Allergy and Personal Protection Equipment), they are just providing a school-like program with support of a corporate medical doctor and Environmental Health and Safety group. They have introduced a web-based education program related to the use of the animal facilities, so that all newcomers can get education right at their desks and certification through passing the test. For the education and training program related to animal experiments, etc., and the handling of laboratory animals is provided only to primary animal handling and procedures (p.o., i.v., so on). For researchers, however, these skills are certified by supervisors and recorded. In addition to these basic education and training programs, it has established the Long-term education program of animal ethics.

Discussion

In the past two decades, the competition among pharmaceutical companies for launching new drugs to market has become increasingly intense year by year. PhRMA, on its Japanese home page (http://www.phrma-jp.org/images/uploads/PhRMA_Facts_200709.pdf), said one new drug will involve from 5,000 to 10,000 candidates. To turn out just one drug requires about a hundred discovery projects or approaches, involving upwards of 7 million compound tests in early screening assays (private data). On these processes, the mode of action and/or safety is confirmed in animal studies; however, it should still involve a thousand or more compounds, and high performance and/or improved performance is demanded at the same time. Therefore, most pharmaceutical institutions tend to devote themselves entirely to set a high throughput screening system to speed up and reduce the costs of the screening process. The way to realize it, then, is *in vitro* studies, in which molecular biologic or genomic procedures are used even in studies to confirm the mode of action or safety.

This process tends to accelerate *in vivo* studies to later stages of development, and eliminates an opportunity to conduct animal studies using the whole body. It also increases the demand of hiring researchers who come from molecular biology, especially, genomic science or biologic engineering fields. Consequently, a majority of researchers recognize the existence of animals as just a donor of organs, tissues, or cells, and become completely desensitized to the living animal as a whole. This present situation clearly shows that long-term education, especially focusing on animal welfare and ethics, is essential and indispensable for animal research institutions. In other words, institutions should provide special education programs for self-development, because present research trends tend to treat living animals without contempt, and may disturb an establishment of personality.

There are various opinions on whether institutions should relate the personality development of researchers, but at least in Japan, it still remains an un-discussed matter. In the case of our institution, through the discussion with the director, the Long-term educational program of animal welfare and ethics sponsored by the animal ethics committee has been provided. This educational program was established in 2003 and it was held twice a year. However, the attendance rate of those who work with laboratory animals was not overwhelming because of a voluntary attendance system. To overcome it, a rule was introduced that required attendance once every three years on the animal ethics committee-sponsored education program in order to continue animal handling.

Research directors of pharmaceutical companies have tremendous responsibilities, and I think that to set the original culture in each institution is one of his or her many responsibilities. Therefore, they should always pay attention to the education of its researchers, especially its Long-term education goals for self-development resulting in the setting of a culture. It is clear that he or she is operating under an indescribable amount of pressure. Yet, to neglect establishing a solid culture in the institution could result in the loss of the trust and confidence of our fellow researchers and the public.

Acknowledgement

I acknowledge the helpful comments of Rowland J. Kinkler (Pfizer R&D) and Ikuo Horii (Showa University) – this paper is the better for their input, however, responsibility for the opinions expressed herein rest with me.

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