Current State & Future Aspect of Animal Welfare of Laboratory Animals for Drug Development in Pharmaceutical Industries in Japan

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Today, we hardly see people in modern nations dying from such diseases as TB, gastroenteritis, pneumonia, and peptic ulcer. Even cancer is not as deadly as before. Medical drugs have been playing a key role in treating and preventing such diseases, and animal tests are an integral part of making such drugs. In animal tests, we lab animal users are always keeping in mind the principle of 3R's (Replacement, Reduction, and Refinement) to respect animal lives and keep their suffering and stress to a minimum. Animal testing facilities comply with laws and regulations on treating and keeping lab animals: they put in place internal regulations conforming to animal testing guidelines specified by leading life science societies. Internal animal test review systems have also been established in many facilities. The number of animals used for testing has been reduced thanks to the ICH international guidelines, which are aimed at improving data quality while minimizing the number of experiments through standardizing testing conditions and methods.

These regulations and guidelines help promote lab animal welfare while improving efficiency and quality of research activities, as they demand a close scrutiny of the necessity of experiments.

Meanwhile, today's social needs for information disclosure require us to communicate more with the public concerning our efforts for lab animal welfare. In this respect, our test data have been made publicly available through journals and other media.

Also in Japan, all research facilities conducting experiments for New Drug Application receive governmental audits. This scheme has been helping improve the quality of animal facilities as well as research facilities.

In spite of these commitments on the research front lines, however, it is also true that some still raise issues of animal testing, calling for stricter control and even a ban thereof. It is my belief that Japan Pharmaceutical Manufacturers Association (JPMA) is obliged to commit itself to the welfare of lab animals and to respond to those questions raised concerning animal protection. JPMA in August 2002 conducted a survey on its member companies for their efforts toward animal welfare. The survey asked: 1) the status of husbandry arrangements for their lab
animals; 2) activities of the lab animal ethics committee within their research facilities; 3) training on animal tests. As a result, it was found that most of the member companies have in place a group dedicated to husbandry of lab animals as well as internal codes on animal welfare. It was also learned that many of them have an animal ethics committee, recommended by the Japanese Association for Laboratory Animal Science. These companies also provide relevant training. However, some companies were found to be inadequate in recording their 3R's activities. The level of each committee's activities and training also varies from company to company.

Based on these results, JPMA is studying the way pharmaceutical companies should be in connection with animal ethics committees.

JPMA is committed to the establishment of best research practice to conduct animal tests critical for drug research and development with the endorsement.
Experience of AAALAC Accreditation in the United States

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SNBL U.S.A., Ltd., a wholly owned subsidiary of Shin Nippon Biomedical Laboratories, Ltd., Kagoshima, Japan, opened its pre-clinical research facility in Washington, USA in 1999. The facility occupies approximately 110,000 ft² (approximately 9,800 m²), one of the largest non-human primate facilities in North America. Drawing on 47 years experience with laboratory animals in Japan, SNBL USA has established a high quality animal facility and operations program to meet strict regulations in the United States, and received full accreditation by AAALAC in 2000.

In the United States, most major animal facilities participate voluntarily in AAALAC's program to demonstrate their commitment to responsible animal care and use.

AAALAC is a private nonprofit organization that promotes the humane treatment of animals in science through a voluntary accreditation program. AAALAC stands for the "Association for Assessment and Accreditation of Laboratory Animal Care."

AAALAC changed its name to the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) in 1996. The name change reflects the organization's growth in other countries, and its commitment to enhancing life sciences and quality animal care around the world.

In the AAALAC accreditation process, research institutions are reviewed to determine whether their laboratory animals care and use are in accordance with "Guide for the Care and Use of Laboratory Animals, 1996, National Research Council." This "Guide" consists of four chapters. The first chapter "Institutional Policies and Responsibilities" focuses on monitoring of the care and use of animals, veterinary care, personnel qualifications and training, and occupational health and safety. Chapter 2, "Animal Environment, Housing, and Management" provides recommendations for housing and environment, behavioral management, husbandry, and population management, including discussions of cage requirements, temperature, humidity, ventilation, lighting and noise control and monitoring. Chapter 3, "Veterinary Medical Care" discusses veterinary medical care and responsibilities of attending veterinarians; it includes recommendations on animal procurement and transportation, preventative medicine, surgery, pain and analgesia, and euthanasia. Chapter 4 discusses the physical plant, including functional
areas and construction guidelines. This book provides research institutions with extremely useful guidelines for establishing and performing animal care and use program. Since its opening, SNBL USA has focused on development and refinement of its own Institutional Animal Care and Use Committee (IACUC) and an occupational health program according to the "Guide". Prior to site visits and evaluations by AAALAC evaluators, research institutions submit a "Description of Institutional Animal Care and Use Program". Dates of site visits are negotiated with the institutions in advance. After an institution earns accreditation, it must report any changes to the animal use program or facility, and the annual number of animals used. Institutions must be re-evaluated every three years in order to maintain their accredited status. After receiving accreditation in 2000, SNBL USA underwent re-evaluation in 2003 and there were no significant findings by IACUC evaluators. An institution could face revocation of its accreditation if a significant problem is found in the re-evaluation process. The IACUC plays a critical role in AAALAC accreditation. The IACUC should include: a veterinarian who is certified or has training or experience in laboratory animal science and medicine or in the use of the species in question; at least one practicing scientist experienced in animal research; at least one member who does not belong the research institution; and at least one member to represent the public community interests in the proper care and use of animals. The IACUC reviews the animal care programs and inspects animal facilities and activity areas at least once every 6 months in accordance with the "Guide". The IACUC's responsibilities include reviews of animal care and use protocols for the rationale and purpose of the proposed use of animals, adequacy of training and experience of personnel in the procedures used, and appropriate methods of sedation, analgesia, and anesthesia. I hope that by explaining SNBL U.S.A.'s experience with AAALAC and our IACUC it can be of some help in promoting better animal care and use or in obtaining AAALAC accreditation for animal facilities in Japan.
Perspectives of the Assessment System by a Third Party

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Animal experimentation is regulated and protected by laws in Japan. The Law for the Humane Treatment and Management of Animals specifies the responsibility of the owner of the animal, and calls for the alleviation of pain and distress as well as the humane death of animals used for scientific purposes. However, the designation of an institutional animal care and use committee (IACUC) and registration of laboratory animal facilities are not stipulated. The Law is supplemented by an administrative ordinance and guidance. Scientific associations concerned have formulated voluntary guidelines for individual research fields to encourage members to balance science and animal welfare. Thus, animal experiments in Japan are self-regulated by a legal and scientific matrix to encourage flexible animal research. Scientists observe animal welfare practices without the force of law but with a moral sense.

To ensure a convincing self-regulation system, we should prepare written documents on institutional policies and responsibilities for animal experiments as well as institutional guidelines on the care and use of laboratory animals. The guidelines should include a performance-based approach so that well-trained laboratory animal scientists can give research personnel advice and the IACUC can evaluate procedures if they are compatible with animal welfare. Also we should define the role and authority of the IACUC for effective self-regulation.

In addition to these efforts by each institution, validation of self-regulation will be important. I would like to propose an assessment and accreditation system for the institutional laboratory animal care and use program. The system should be offered by a third party. The third party organization will send site visitors to the applicant institute after receiving an application. The purpose of the site visit is to assess the adequacy of the self-regulation system and its practical use from the viewpoint of laboratory animal scientists. The following points should be discussed regarding the assessment and accreditation system.

1. Guidelines for assessment: Preparation of guidelines compatible with national regulations and to harmonize with the international guiding principles. Also a guide for site visitors and standards for assessment will be necessary.
2. Organization: Operation as an NPO. Administration by existing associations in the field of
laboratory animal science might cause misunderstanding about their neutrality.

3. Merit of accreditation: A means to facilitate international R&D collaboration. A linkage with the national grant-in-aid system may give the accredited institution an advantage for receiving research funds.

Assessment by the third party is conducted as a peer-review. The accreditation will prove the ethical and scientific adequacy of animal experimentation to gain public support for the institute and the researchers.