1. Introduction

In regard to the use of experimental animals for research and education, alternative methods for animal testing came to be discussed on account of criticisms made on animal welfare and humanitarian grounds as well as awareness among scientists. In 1954, Russell and Burch suggested the 3R’s principles, regarding alternative methods to animal testing. In Britain, Fund for the Replacement of Animals in Medical Experiments (FRAME) was founded in order to promote the research in this field and social recognition. In the United States, Johns Hopkins Center for Alternatives to Animal Testing (CAAT) was established in 1981. In Japan, on the other hand, Professor T. Sugawara at Kyoto University launched a research group in 1982, which later became JSAAE. A number of alternative methods to safety tests have been developed through these activities EU accordingly established ECVAM in 1991 (opened in 1994) as a base for development of the alternative methods, in order to set up and maintain databases of the alternative methods and to encourage communications among consumers, animal rights groups and scientists in governmental agencies, industry and biology/medicine areas.

ECVAM in 1991 (opened in 1994) as a base for development of the alternative methods, in order to set up and maintain databases of the alternative methods and to encourage communications among consumers, animal rights groups and scientists in governmental agencies, industry and biology/medicine areas.

Fig 1 International Center for the validation of alternative methods
In the United States, ICCVAM was established under NICEATM in 1993, consisting of 14 governmental agencies and research institutes including NIEHS, in order for the federal government to deal with issues regarding development, validation and incorporation of toxicity test methods as well as domestic and international harmonization. European governmental agencies are currently working on incorporation of newly developed alternative methods, which have been proven feasible by scientific evaluation. Specifically, ECVAM and ICCVAM are considering possibilities of incorporating governmental tests involving new technology such as toxicogenomics as well as requirements of new toxicological evaluations such as quantitative structure activity relationship and investigations of endocrine disrupting chemicals, in addition to conventional alternative methods for safety tests. GLP standard to guarantee the credibility of results of in vitro safety test methods has also been discussed, and position paper was prepared at OECD level. Moreover, EU government and legislature promulgated the 7th revision of Cosmetic Directive as of March 2003, which will ban animal testing in principle for safety evaluation of cosmetics by 2009. Ever since the launch, JSAAE has been dedicated to validation and evaluation of alternative methods to animal testing, and it has helped researchers exchange information and continued communication with the public, through research support by means of funding, research presentations at conventions and symposiums, education of alternative and ethical animal testing and lectures for the public. JEAAE also plans to hold the 6th World Congress on Alternatives and Animal Use in Life Sciences in Tokyo, in 2007. This convention will be held in the critical time toward banning, in principle, animal testing for safety evaluation of cosmetics in the EU, when the research results will be summarized and required research plans will be prepared.

2. Necessity of research/evaluation center for the alternative methods in Japan

ECVAM and ICCVAM have come to cooperate in collaborative validation and mutual recognition of evaluation results. They also call for assistance from Japan. On the other hand, in Japan,
JSAAE-centered development of the alternative methods, validation studies, validation and preparation of draft plan for alternative methods for eye irritancy tests (Ohno, 1999) and evaluation of alternative methods for 3T3-NRU phototoxicity tests (Ohno et al., 2005) have been supported by Health, Labor and Welfare Sciences Research Grants. Activities in progress also include validation and evaluation of improved alternative methods for phototoxicity tests, validation and evaluation of alternative methods for dermal corrosivity tests, validation of alternative methods for dermal irritancy tests and validation of improved methods for LLNA (Local Lymph-Node Assay). However, an institute specialized for the alternative methods such as ECVAM and ICCVAM was not available then, and international cooperation among public institutes was not practical. Currently, Japan is behind in validation and evaluation of original test methods, and international recognition is thus hard to achieve. Therefore, Japan also needs to have a center for alternative method research, Japanese Center for Validation of Alternative Methods (JaCVAM), in order to perform research and development of new test methods in vitro, use the professional knowledge for validation and evaluation of new alternative methods and act internationally (Fig.2). Nonetheless, securing the financial and human resources of the European level is not feasible, and, therefore, collaborations with related academic associations and industry are desirable.

Evaluation of new alternative methods by JaCVAM can be divided in 2 steps of evaluation by an evaluation committee mainly composed of specialists and evaluation by a board of clinicians, toxicology specialists, government staff, and so on. Also, as for a test method that lacks an adequate amount of validation data and yet evaluated as valuable, validation of an international level should be made possible through a support from the related academic associations and industry. It is necessary to cooperate with Japanese Society of Alternatives to Animal Experiments (JSAAE) and Japanese industry group like Japanese Cosmetic Industry Association (JCIA). JSAAE is the only scientific community that is specified to research on alternatives. It has been contributing to the communication between scientists and animal protection groups during these 20 years.

Research group supported by the Ministry of Health, Labor, and Welfare has been cooperating with JSAAE to develop and evaluate new alternative methods. As a result, the new test methods conforming the 3R's objectives are expected to be further supported along with following positive anticipations:
1) The international-level validation sponsored by JaCVAM will clarify the advantages and limitations of the new test methods, and the safety evaluation level of drugs, cosmetics, agrochemicals and other chemical substances will consequently improve;
2) Using appropriately evaluated and economically advantageous methods will accelerate the safety evaluation process;
3) Appropriate evaluation of safety test methods incorporating new methods and ideas such as toxicogenomics and proteomics will encourage their use;
4) Development of the alternative test methods in collaboration with ECVAM and ICCVAM will be an international contribution to development of new test methods; and furthermore,
5) The attitude and contribution of our country toward development of alternative methods for animal testing will be acknowledged.

References


Corresponding author:
Yasuo Ohno, Ph.D.
Deputy Director-General,
National Institute of Health Sciences.
1-18-1, Kamiyoga, Setagaya, Tokyo 158-8501, Japan.
tel: +81-3-3700-1141 ext 201, +81-3- 3700-2859
fax: +81-3-3700-1340
E-mail: ohno@nihs.go.jp