

Invited Mini Review

## Searching and review on the Three Rs information in Korea: time for quality assessment and continued education

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Scientists planning research that involves the use of animals are required by international and/or national law to examine the possibilities for the implementation of Replacement, Reduction and/or Refinement (the Three Rs principles of Russell and Burch) in experiments for research, testing, and education. There are two Korean laws legislating humane use of animals and ethical review prior to animal experiments. This report reviews current practice of the literature search by the researchers and protocol review by the Institutional Animal Care and Use Committees on the Replacement, Reduction and Refinement alternatives in Korea. The promotion and protection of the laboratory animals are one of the core competencies of investigators exploring the ethical conduct of research and good science. [BMB Reports 2013; 46(7): 335-337]

### INTRODUCTION

In many countries, scientists and educators planning research that involves the use of animals are required by law to examine the possibilities for the implementation of *Replacement*, *Reduction* and/or *Refinement* alternatives in these experiments (1). There are two laws that govern animal experiments in Korea: the *Animal Protection Act* (APA), and the *Laboratory Animals Act* (LAA) (2). Both laws impose the humane use of animals in science (3), by applying the Three Rs principles of Russell and Burch (4). Russell and Burch defined alternative procedures as the Three Rs: the *Replacement* of animals with non-animal models or species lower on the phylogenetic scale; the *Reduction* of the number of animals used; and/or the *Refinement* of techniques to reduce or eliminate unnecessary pain or distress to laboratory animals (5). Both laws also require the mandatory establishment of Institutional Animal Care and Use Committees

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(IACUCs), and ethical review prior to animal experiments that are conducted in research, testing and education. The role of the APA's IACUCs (Animal Experimentation Ethics Committees) (6) differs from that of the LAA's IACUCs (Animal Experimentation Operating Committees) (7).

The objectives of this review paper are to provide a brief overview of the current practice of the literature search for Replacement, Reduction and Refinement alternatives by Korean researchers and IACUCs, and to propose the consideration of quality assessment and continued education.

### Current practice on the literature search for the Three Rs alternatives

There are tremendous amount of information available from international websites (5); however, it is very difficult to obtain the specific information desired (8). There are few Korean websites providing information on the Three Rs; such as the Korean Society for Alternatives to Animal Experiments (<http://www.ksaae.org>), the Institute for the 3Rs at Konkuk University (<http://threers.konkuk.ac.kr/>), and the Korea National Information Center (<http://3r.animal.go.kr>). The authors are involved in initial development of two websites (2, 9), but the services provided are limited at this moment.

There are sufficient alternatives available at relatively low-cost, and with proven educational efficacy, to allow the vast majority of students who study biomedical science courses to qualify without using animal experiments (10, 11). However, resources and information on the Three Rs are inadequate to comply with the requirements (2) in Korea. Based on our research on the attitudes assessment of Korean veterinary professors and students towards animal use and alternatives in their laboratory classes in Korea from 2007 to 2010, professors using animals had too little knowledge (7.8%) of the resources and information on the Three Rs to comply with the requirement. They (75.5%) were not aware of the Three Rs concepts and available teaching resources. Only nine of the 133 professors (6.8%) were applying the principles of the Three Rs in their teaching (Paper submitted). Alternatives to the use of laboratory animals are often viewed as supplementary educational teaching aids, rather than as replacements for animals (9).

The principal investigators who propose to use animals in their research must demonstrate to IACUCs by a current liter-

ature search that they have considered alternatives (5). The IACUCs have responsibility for ensuring that applicants made an effort conducting a current literature search to determine if the Three Rs alternatives are available: to substitute the proposed animal use, to avoid unnecessary duplication, and to describe humane procedures if the proposed study involves pain or distress (5). Based on our national survey (Paper in progress) towards Korean IACUC members and researchers in 2012, assessing literature search practice to comply with the Three Rs alternatives, 85 (12%) respondents had no experience of literature search of the Three Rs alternatives. 182 (25%) respondents were not aware of how or where to find the alternatives to animal use, or more humane procedures to painful or distressful procedures (5). Further, 647 (72%) respondents used PubMed (Medline) and Google search engine to search for Three Rs alternatives, which usually generates unnecessary duplication, which could be avoided. The US Department of Agriculture discourages IACUCs from using Google as a database because of the searching behaviors that are common amongst people searching the web for information.

#### **Education on the literature search for the Three Rs alternatives**

Educating scientists and IACUCs is key to helping them embrace the use of alternatives and showing them that useful information is available is a good place to start. Training and instruction of personnel are important components of animal care and use programs, because they help to ensure the health and welfare of the animals, and the integrity of the research or testing results (5). Based on our national survey (Paper in progress) towards Korean IACUC members and researchers in 2012, assessing literature search practice to comply with the Three Rs alternatives, 487 (68%) respondents did not have the education opportunity to conduct an alternative Three Rs search.

## **DISCUSSION**

Under the Korean Laboratory Animals Act Chapter 5, Article 17 (7), the Korea Food and Drug Administration shall conduct necessary education and training and/or assign responsibility to research facilities, to provide for the training of scientists, animal technicians, and other personnel involved with animal care and treatment. The United States Department of Agriculture (USDA) regulations require the IACUC to review activities involving animals, and as part of that review, to determine that personnel conducting the procedures are appropriately trained and qualified (9 CFR 2.31; CFR 1989, 2006) (12). The USDA has also issued several policies that provide additional guidance related to training regarding handling, immobilization, anesthesia, tranquilization, and euthanasia (5, 12). IACUCs and/or individuals are responsible for ensuring that they have the competency and skills to perform their duties properly. IACUC is also responsible for ensuring that an effort was made in good faith to determine whether the Three Rs alternatives and procedures were available to accomplish the objectives of the experiments (5). Our findings on

the current practice towards the literature search and education on the Three Rs alternatives, suggest that Korean guidance and continued education is needed to find more efficient and productive information and resources on the Three Rs alternatives and to meet the requirements of IACUC reviews. The Animal Welfare Information Center, located at the USDA National Agricultural Library, provides information and training to promote the humane care and use of animals (5). Proper education and training also helps to promote the consideration of alternatives, recognition of animal pain and distress, appropriate use of pain-relieving agents, aseptic technique, pre-and post-procedural care, and personnel health and safety (12).

Most databases and searching engines run in English, such as PubMed, MEDLINE (US National Library of Medicine, Altweb, FRAME, ECVAM (13) and Go3R ([www.go3r.org](http://www.go3r.org)). The US Department of Agriculture discourages IACUCs from using Google as a database because of the searching behaviors that are common amongst people searching the web for information. The US Animal Welfare Act provides a guideline of sources to be consulted, such as Biological abstracts, Index Medicus, the Current Research Information Service (CRIS), and the Animal Welfare Information Center that is operated by the National Agricultural Library (5). Korea also established a National Information Center for the 3Rs, the KNIC3Rs providing in the adequacy of a facility's training program for the protection of animals used for scientific purpose.

Legislations governing animal experiments vary among countries. Close collaboration between government, academia and industry is essential for the formulation of evidence-based education policies (8). A Korean guidance and education resources platform is necessary to facilitate how to search for information on the Three Rs, and their implementation, especially in a non-English speaking environment.

## **LIMITATIONS AND CHALLENGES**

Research data on the attitudes assessment of Korean veterinary professors and students towards animal use and alternatives in their laboratory classes in Korea may not reflect current practice. It is about time to conduct another survey monitoring the current practices of Korean veterinary professors and students.

## **RECOMMENDATIONS**

While most scientists are aware of the requirement, many have no idea how to comply with it. In order to further improve and facilitate access to available Three Rs information, a close compliance evaluation should be assessed on the gap between the statutory requirement need to apply the Three Rs concept, and the adequacy of a facility's training program. Training in proper search techniques and user-friendly systems for practical application for the Three Rs are vital to comply with the requirements of the Korean Animal Protection Act and/or Korean Laboratory Animals Act. It is recommended to proactively lead scientists

and lay members in locating information on the Three Rs by the government website of the KNIC3Rs (<http://3r.animal.go.kr>). The promotion and protection of the laboratory animal is one of the core competencies of investigators exploring the ethical conduct of research. It is time to develop Korean guidance, and to promote an educational resource platform to facilitate how and where to search for the information on Three Rs alternatives, and to make searching for the Three Rs methods more effective.

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