

Invited Mini Review

Individual and collective responsibility to enhance regulatory compliance of the Three Rs

Byung In Choe* & Gwi Hyang Lee

Division of Institutional Review and Research Ethics, Nicholas Cardinal Cheong Graduate School for Life, The Catholic University of Korea, Seoul 137-701, Korea

Investigators planning to use animals in their research and the Institutional Animal Care and Use Committee (IACUC) members who review the research protocols must take personal responsibility for ensuring that they have the skills and knowledge to perform their duties, applying the Three Rs principles of Russell and Burch. The two Korean laws introduced in 2008 and 2009 regulating animal use for scientific purposes in line with the Three Rs principles have been revised a total of 11 times over the last 6 years. Both regulatory agencies, e.g., the Animal and Plant Quarantine Agency and the Ministry of Food and Drug Safety, provide regular training based on the legal requirements. Based on the amended Animal Welfare Act, the IACUC appointment framework has been upgraded: appointments are now for two-year terms and require a qualified training certificate issued by the Animal and Plant Quarantine Agency since 2012. The authors reviewed the current curricular programs and types of training conducted by the two governing agencies through Internet searches. Our Internet survey results suggest that: a) diversity should be provided in training curricula, based on the roles, backgrounds and needs of the individual trainees; b) proper and continued educational programs should be provided, based on trainees' experiences; and c) active encouragement by government authorities can improve the quality of training curricula. [BMB Reports 2014; 47(4): 179-183]

INTRODUCTION

Driven by both scientific needs and public concerns relating to animal welfare and use, the last decade has seen government support for the implementation of a national policy directed to the protection of animals used for experimental and other scientific purposes. There are two Korean laws, the Animal

Protection Act (hereafter, the APA) and the Laboratory Animal Act (hereafter, the LAA), which legislate the humane use of animals and the protocol review by the Institutional Animal Care and Use Committee (hereafter, the IACUC). Both laws impose the Three Rs principles of *replacement*, *reduction*, and *refinement* in animal experiments for research, testing and education (1). The implementation of the Three Rs principles when performing animal studies in Korea requires that all personnel involved in laboratory animal care and use have the proper education, training and experience (2). Two Korean laws governing animals use have been revised a total of 11 times over the last 6 years. Even when animal use is tightly regulated and supervised, the individual researcher's responsibility in the implementation of the 3Rs is still decisive (3). Our survey findings conducted in 2012 on the current practice towards the literature searches and education on the Three Rs alternatives suggest that many researchers and IACUC members may not possess the expertise that is required to perform an efficient, yet effective literature or Internet search, in the attempt to locate relevant information on the Three Rs alternatives. Such searches may be seen as a burden by some, particularly when inefficient search strategies do not efficiently or reliably find the relevant information (2).

Although training programs conducted by government and institutions aim to raise researchers' awareness and increase their knowledge, their effect on scientists' attitudes and practice has not so far been systematically assessed (3). The authors reviewed current training curricula and types of training programs conducted by two Korean governing regulatory agencies through an Internet search. This report presents the findings of an Internet survey on the a) legislation governing animal use in Korea; and b) program curricula and types of training conducted by two governing regulatory agencies; the Animal and Plant Quarantine Agency (hereafter, the QIA) and the Ministry of Food and Drug Safety (hereafter, the Korea FDA).

METHODS

The authors systematically extracted and evaluated information on the legislation governing animal use in Korea, and the training program curricula and types of training from each of the authorized official websites. The Internet survey

*Corresponding author. Tel: +82-2-2258-7395; Fax: +82-70-4099-7884; E-mail: bichoe@catholic.ac.kr

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was focused on an overview of the law and policy towards animal use, and the associated education and training programs. The cited websites are: a) the Korea Ministry of Government Legislation (4); b) the Animal and Plant Quarantine Agency (5); and c) the Ministry of Food and Drug Safety (6). These citations were updated on February 7, 2014.

RESULTS

Legislation governing animal use and a training mandate in Korea

The policy objective and purpose of the “Animal Protection Act” is to enhance public health, sentiment and confidence, through an effective system minimizing animal cruelty and promoting animal welfare. When performing animal studies, all personnel are required to have the proper education, training and experience. The APA has been amended nine times since first applying the Three Rs principles in 2008 (7).

The purpose of the “Laboratory Animal Act” is to contribute to the development of life sciences and improvement in public health by enhancing the ethics and reliability of animal research and testing, through appropriate regulation and oversight of institutions, laboratory animals and animal testing. Under the Korean Laboratory Animals Act (Chapter 5, Article 17) (8), the Korea FDA provides necessary education and training, and/or assigns the responsibility to the research facilities to provide for the training of scientists, animal technicians, and

other personnel who are involved with animal care and treatment (9). The LAA has been amended four times, since applying the Three Rs principles in 2009. In 2012, the LAA IACUC was harmonized with the APA IACUC to prevent unnecessary duplication of workloads and minimize the regulatory and administrative burdens. Table 1 provides details of the consolidated data on the legislation governing animal used for scientific and experimental purposes.

Program curricula and types of training

Both regulatory agencies conduct regular training courses, based on their legal mandate. The training course conducted by the QIA consists of four programs, with a total duration of 4 hours. The QIA training target group is mainly IACUC members seeking initial qualification. The training course conducted by the Korea FAD is comprised of five programs and 11 modules, and is with a total duration of 6 hours. The consolidated data on the course programs conducted by the regulatory agencies are detailed in Tables 2 and 3.

The annual trainings provided by both regulatory agencies were mostly of the ‘Instructor-led training’ type. Two joint workshops oriented towards the Korea Institutional Animal Care and Use Committee members and researchers in 2012 and 2013, with the “Korea National Information center for the 3Rs” conducted by QIA, were focused on interactive training, including case studies (2).

Table 1. Comparison of the QIA and the Korea FDA animal use regulations

Category	Registration governing animal use and education	
Legislation on animal use	Animal Protection Act (Law 8282 / 2008.1.27)	Laboratory Animal Act (Law 9025 / 2009.3.29)
Number of revisions/Last revision	Nine times (Law 12051 / 2014.8.14)	Four times (Law 11987 / 2013.7.30)
Responsible regulatory authority	Animal and Plant Quarantine Agency, Ministry of Food, Agriculture, Forestry and Fisheries	Ministry of Ministry of Food and Drug Safety
Regulating the 3Rs principles and ethical review	IACUC- Scientific and ethical review committee (Law Chapter 3 Articles 23, 25)	IACUC- Animal Experimentation Operating Committee (Law Articles 5, 7, Regulation Article 4)
Compliance oversight scope	Corporation, Organization and Institution conducting animal experiments (Law Article 2, Regulation Article 4)	Registered institutions for the purpose of the production, import, and sales of laboratory animals (Law Article 8, Regulation Article 2)
Qualification of the IACUC Education	(Law Article 27, Enforcement 26) (Regulation Article 11, Enforcement 26)	(Regulation Article 4) (Law Articles 5, 6, 17)

Table 2. Comparison of the QIA and Korea FDA training course programs

QIA	Korea FDA
Animal Protection Act and welfare policy	Essential components of regulations on laboratory animal
Concept and international update on animal protection and welfare	Operation and management of the animal facilities
Scientific and ethical use of laboratory animals	IACUC
Planning protocol and review tips	Quality management of the Lab animal
N/A	Welfare and ethics of the Lab animal use

Table 3. Comparison of the QIA and Korea FDA training participants/enrolled and duration

Organizer	QIA			Korea FDA			
	Year	Numbers of participants	Yearly conducted training	Duration (hour)	Numbers of enrolled applications	Yearly conducted training	Duration (hour)
	2009	82	2 times	4	983	4 times	4
	2010	168	2 times	4	857	5 times	4
	2011	164	4 times	4	1,024	5 times	4
	2012	132	4 times	4	829	5 times	6
	2013	N/A	4 times	4	843	5 times	6

DISCUSSION

Legislations governing animal use in Korea

Two Korean laws governing animals use have been revised a total of 11 times over the last 6 years. The latest technology and scientific progress have produced many alternative methods to replace, reduce and refine animal use. The Government should include proper educational guidelines and training to clarify the requirements and ensure consistency of practice and compliance. The QIA training target group is mainly IACUC members seeking initial qualification at the institutions conducting research using animals (the APA Article 2, Regulation Article 4). However, there is no legal requirement to have or document continued or refresher training for the IACUCs and researchers to update their knowledge. 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). The USDA has also issued several policies that provide additional guidance related to training regarding handling, immobilization, anesthesia, tranquilization, and euthanasia (9).

Under the Korean Laboratory Animals Act (Regulation Article 2), the Korea FDA limits its inspection to the animal facilities registered to the Korea FDA and only conducts necessary education and training, and/or assigns the responsibility to the research facilities to provide for the training of scientists, animal technicians, and other personnel who are involved with animal care and treatment (9).

The regulations that affect animal use in education are contained within laws regulating animal use in research and testing. Such laws usually do not apply to animals used for dissection at schools, where students are rarely aware of the laws. Humane care in Korea and elsewhere does not apply to dead animals: for example the humane killing of animals for dissection is not defined as a “procedure” in the United Kingdom (10) or elsewhere in Europe. Furthermore, there are no national laws against the killing of animals for dissection in pre-college education (e.g., primary, middle, high school and private educational institutes) in Korea. Both regulatory agencies

carry out their compliance inspection within the framework of the law, which include the higher education institutions conducting animal experiments (the APA Article 2, Regulation 4.8) and registered institutions for the purpose of the production, import, and sales of laboratory animals (the LAA Article 8, Regulation Article 2). These issues should be addressed when the next opportunity arises to amend the legislation. Legislation and regulations related to using animals and dissection in the United States are a complex array of educational guidelines and standards which are commonly regarded as being in the oversight of national, state, and local districts oversight laws (11).

It is the individual and collective responsibility of the government and institutions to meet the minimal requirements stipulated by applicable laws, regulations, and policies. Each organization and individual that plans to use animals in research must be committed to complying with the laws and regulations that govern the conduct of animal research, and to upholding the highest ethical standards. It is the responsibility of the principal investigator to enforce the institutional requirement for animal research training certification, for personnel who are listed as study team members, on a research project initiated at the institution before the submission of the research protocol that is to be reviewed by the IACUC. The IACUC and/or individuals are responsible for making good faith efforts to determine whether the Three Rs alternatives and procedures were available, to accomplish the objectives of the experiments (12). The IACUCs and/or individuals are also personally responsible for ensuring that they have competency and skills to perform their duties properly. The IACUCs are also required to demonstrate a certification of animal care and use training conducted by the QIA for initial qualification.

Organizations must comply with the regulations and official guidelines (e.g., the QIA and/or Korea FDA). It is time that both government and research organizations choose to establish more extensive and effective training programs for personnel to ensure the humane care and use of animals, to better support their scientific mission, and to optimize the management of animal care and use programs to enhance regulatory compliance with the Three Rs (9).

The legislation governing animal experiments varies among

countries. 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. Close collaboration among government, academia and industry is essential for the formulation of evidence-based education policies (13). Our findings on the current practice towards the literature search and education on the Three Rs alternatives suggest the need for a Korean guidance and continued education platform, to more efficiently and productively find information and resources on the Three Rs alternatives, especially for a non-English speaking environment (2). The survey results of the Portuguese scientists who participated in Laboratory Animal Science training, toward their attitude change as regards applying the 3Rs principles, suggest that such courses are effective in promoting awareness and increasing knowledge of the 3Rs, particularly with regard to refinement. However, participation in the courses did not of itself change perceptions on the current and future needs for animal use in research (3).

Program curricula and types of training

For the last five years, training course programs and topics have been mostly general and descriptive. The topics need to focus more specifically on the role of the research group (e.g., investigators and research staffs, IACUC members and coordinators, institutional officials and compliance personnel, and regulators and animal advocates), and the experience of the training group. The practical topics and educational sessions should prove of benefit in overcoming the current challenges in the field, and provide regulatory updates for the experienced groups. Related national and international laws and policies are often revised as progress is made and the effectiveness of current policy and practice is reviewed. Accordingly, a collaborative team of field experts to design and implement continued education programs for the experienced groups should be assembled, to identify and promote up-to-date knowledge, and develop or select informative practical case studies (14). Refresher courses should be considered every 2 years. Accreditation of training courses and training certificates with continuing education credits from various professional associations may be beneficial for both the individual's interests and the institution's requirements of the qualifying continuing education activities. The training or workshops organized by the government agencies should emphasize simple, efficient and effective processes that personnel can utilize and which monitors and auditors can use to help them to measure and improve their performance. Institutions should consider undertaking a gap-analysis comparing the statutory requirements that mandate the application of the Three Rs concept, and the measures they have in place for the protection of animals used for the scientific purpose including the adequacy of a facility's training program (15).

Both regulatory agencies mostly offered 'Instructor-led train-

ings' and off-line trainings. They provide a one-day training course tailed to geographic regions and announce fixed dates a couple of months ahead through their website notice board. Educational opportunities should be provided, when they are needed. Workshops involving recognised experts in the field of interest have proved particularly useful in defining areas of concern, making practical recommendations for action, and providing impetus and clarification, so that interested groups can act on the recommendations. This will provide an opportunity for representatives from the interest areas to bridge expert advice and quality education, and offer support resources to Korean scientist and researchers. Web based teaching environments are a feasible learning method. The Food and Agriculture Officials Training Institute offers a web-based cyber training course with the title of animal welfare and laboratory animal ethics. This training is mainly for government officials, but is also open to scientists and the public. However, these courses are limited as to dates and number of learners. Online courses, like the CITI Program (16), will be accessible for learning, based on an individual's schedule, and interest in the topics.

LIMITATIONS AND CHALLENGES

This review describes selected laws and regulations impacting animal research conducted at the animal testing and laboratory animal production facilities. The data obtained from the Internet through government websites is limited, and may not reflect up-to-date activities and best practice, such as sponsoring training programs, or collaborating with other organizations. These limitations should be taken into account in the future when planning government policy and service delivery.

CONCLUSIONS

The promotion of the Three Rs and the protection of animals used for research and testing are core competencies of investigators performing ethical research. Training programs for the Three Rs are vital to comply with the requirements of Korean Animal Protection Act and/or Korean Laboratory Animals Act. Training course programs and curricula should include practical, immediately usable tools, strategies and techniques that can be applied by research institutions and scientists. It is recommended that steps be taken to develop a trainer-of-trainers workshop for institutions and their staff, to establish and continuously update and improve instruction programs in animal research ethics. It is recommended that a workshop be organized in collaboration with the annual trainer-of-trainers to enable the identification and sharing best practice locally, nationally and internationally. Gaps between the statutory requirements that mandate application of the Three Rs concept, and the adequacy of a facility's training program should be identified and remedied. Training certificates and continuing education (CE) credits from various professional associations

may be beneficial for both the individual's interest, and the institutional requirement of the qualifying continuing education activities. It is recommended that a monitoring mechanism for institutions, to annually report the education and training programs they conduct, be introduced as a part of compliance activity. Our Internet survey results suggest that: a) diversity should be provided in training curricula, based on each individual's background, role and needs, e.g., researcher, IACUC scientific member, non-scientific member; b) proper and continued educational programs should be provided, based on the learners' needs and experiences, e.g., a basic course for the beginner group, a refresher course for continuing members, and an advanced course for selecting different kinds of laboratory animal species; and c) active encouragement by government authorities can improve the quality of training curricula.

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REFERENCES

1. Lee, G. H., Choe, B. I., Kim, J. S., Hart, L. A. and Han, J. S. (2010) Current status of animal use and alternatives in Korean veterinary medical schools. *ATLA* **38**, 221-230.
2. Choe, B. I. and Lee, G. H. (2013) Searching and review on the Three Rs information in Korea: time for quality assessment and continued education. *BMB Rep.* **46**, 335-337.
3. Franco, N. H. and Olsson, I. A. S. (2014) Scientists and the 3Rs: attitudes to animal use in biomedical research and the effect of mandatory training in laboratory animal science. *Lab. Animal.* **48**, 50-60.
4. Korea Ministry of Government Legislation. <http://www.law.go.kr> (Accessed 2.7.14).
5. Animal and Plant Quarantine Agency. <http://aec.qia.go.kr> (Accessed 2.7.14).
6. Ministry of Food and Drug Safety. <http://www.mfds.go.kr> (Accessed 2.7.14).
7. Animal Welfare Act. <http://www.law.go.kr> (Accessed 2.7.14).
8. Laboratory Animal Law. <http://www.law.go.kr> (Accessed 2.7.14).
9. Anderson, L. C. (2007) Institutional and IACUC Responsibilities for Animal Care and Use Education and Training Programs. *ILAR J.* **48**, 90-5.
10. Balcombe, J. (2000) A global overview of law and policy concerning animal use in education. In *Progress in the Reduction, Refinement and Replacement of Animal Experimentation* (ed. M. Balls, A-M. van Zeller & M. E. Halder), 1343-1350. Amsterdam, The Netherlands: Elsevier Science BV.
11. Hart, L. A., Wood, M. W. and Hart, B. L. (2008) Why dissection? Animal use in education. 93-109. Westport, Connecticut, the United States of America, Greenwood Press.
12. Neddill, D. and Adams, K. M. (2011) Literature search strategies to comply with institutional animal care and use committee review requirements. *J. Vet. Med. Educ.* **38**, 150-156.
13. Crawford, R. L. and Allen, T. (2008) Databases for biomedical animal resources. In P. M. Conn (ed.), *Sourcebook of Models for Biomedical Research* 49-54. Totowa, NJ: Humana Press Inc.
14. Food and Agriculture Officials Training Institute. <http://www.ati.go.kr> (Accessed 02.25.14).
15. Hudson-Shore, M. (2012) Searching Effectively for Three Rs information. *ATLA* **40**, 22-23.
16. CITI-KOREA. <https://www.citiprogram.org> (Accessed 02.25.14).