



Who is Concerned about Animal Care and Use in Developing Countries?

Francis Adelaide Fakoya

Department of Anatomical Sciences, School of Medicine, St. George's University, Grenada, West Indies

Summary

Many advances have been made to develop and disseminate information and guidelines for the care and use of laboratory animals in many parts of the world aiming to improve the health, welfare, and psychological well-being of the research animals. These advances are based on the Three Rs and also improve the science by increasing the accuracy and reproducibility, and by ensuring quality control of the validity of animal based results. However, this trend is lacking in most developing countries. A comprehensive and systematic review of published reports revealed that forward looking towards alternatives to animal use, e.g., adoption of the 3Rs, oversight by Institutional Animal Care and Use Committees (IACUCs) or ethical committees on animal based research, is not visible in developing countries. These deficiencies may account for the lack of recognition of data from developing countries and the absence of searchable reports that would be comparable to those from the Western world and Far East. In order for developing countries to catch up on this matter, the following issues need to be addressed: advocacy for involvement of governmental regulations, scientifically responsible conduct of research by investigators, institutional commitment to animal welfare in research, as well as exposure to training opportunities by international resource agencies on animal care and use (such as the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) and the Institute for Laboratory Animal Research (ILAR)). These issues must be addressed before increased public awareness of the current deficiencies further slows the pace of scientific advancement in these countries.

Keywords: animal welfare, animal experimentation, developing countries, IACUC, 3Rs

1 Introduction

Global expectations for improvements in the health of humans and animals require scientific studies involving the use of animals while addressing public concerns about the welfare of the animals used in science. However, more than 1.2 billion people live in extreme poverty, about 850 million are chronically hungry (and the number is rising), and most of these people are found in developing countries in sub-Saharan Africa and South and East Asia¹. Yet animal welfare is of importance because of the link between healthy, well-cared-for animals and sound science (Demers et al., 2006). To arrest this trend, the Millennium Development Goals (MDG) of the United Nations set an overall objective to reduce the proportion of people who are extremely poor and hungry by 50% by the year 2015.¹

In developing countries, poverty, resource scarcity, and education all factor into the way that animals are regarded and treated. In some cultures, certain animals may be accorded holy status, while other species are subject to extreme indifference and neglect. Economic systems and human values that place efficiency and profit above animal welfare lead to the inhumane practices found in factory farming (Rahman et al., 2005); thus,

animal welfare issues cannot be viewed in isolation from culture, values, and economic conditions – all of which affect how animals are perceived and treated. Developing countries are increasingly coming under pressure to harmonize international standards set by developed countries, such as to improve their delivery of veterinary services as a prerequisite for entering the competitive arena of international trade in animals and animal products (Bruckner, 2004); the demand of certain standards in the instructions to authors by some scientific journals, e.g., of quality, relevance, and, in animal experiments, proof that no alternative is available (Gruber and Hartung, 2004; Kilkenny et al., 2010; MacCallum, 2010). While consideration of alternative methods for animal tests in developing countries is significantly important (because good quality laboratory animals and proper animal facilities are not always sufficiently available to perform the currently required quality controlled testing), it is to be noted that some alternative methods have been implemented in the development, production, and testing of new vaccines (Di Fabio et al., 2002; Hong and Hendriks, 1999) as well as in toxicological studies by some institutions.

Animal welfare is profoundly affected by the culture, values, and economies of human societies². Research that can cause

¹ United Nations, MDG Report, 2010: <http://www.un.org/millenniumgoals/pdf/MDG%20Report%202010%20En%20r15%20-low%20res%2020100615%20-.pdf> (accessed 04.08.2011)

² International Animal Assistance Network: Internal Animal welfare issues <http://www.internationalanimalnet.org/?q=issues> (accessed 14.07.2011)



pain, suffering, or lasting harm to an animal is very tightly regulated in countries such as the UK, USA, Canada, Australia, and Europe (Blokhuys, 2004; Baumans, 2004). Animals are sentient beings that are capable of experiencing pain and suffering. Even a procedure which is a common part of daily veterinary practice, such as venipuncture to obtain a blood sample, is regulated when it is used for research purposes, as the animal will be exposed to the pain of needle insertion without obtaining any direct benefit from the procedure. Such regulation is in place for the protection of both the animals involved in research and the researchers themselves (Baumans, 2004).

The most common types of animals used in experiments are mice, rats and other rodents, rabbits, birds, and fish. Cats, dogs, pigs, sheep, goats, and primates are also found in laboratories in significant numbers (Baumans, 2004). Thousands of primates are used every year around the world in scientific experiments with baboons, marmosets, macaques, and green monkeys being the most common (Taylor, 2010). The use of chimpanzees still occurs in the US (Conlee, 2008). Conservative estimates place animals bred for and/or used in research at more than 100 million per year globally (Nuffield Council on Bioethics, 2005; Taylor et al., 2008). The major purposes for which research animals are used include: basic and applied medical research (around one-third to one-half); the development of drugs and medical devices (around one-third to one-half); the production and standardization of vaccines and other biologicals (common in the developing world); the safety testing of other chemicals (around one-tenth); educational activities (a relatively small proportion – under 5%); and to diagnose disease and identify pathogens (Baumans, 2004). The pattern of use differs quite dramatically between the developed world (e.g., North America, Europe, and Japan (Ormandy et al., 2009; Takahashi-Omoe and Omoe, 2007)) and developing countries such as India, Indonesia, Brazil, and others. In the developing world, diagnosis, biologicals production, and testing are large users of laboratory animals. This is not the case in Europe and the US, where the pharmaceutical, biotech, and university research centers are the major users (van der Laan et al., 2010). Industries – pharmaceutical, chemical, and biotech – that use large numbers of research animals operate across national boundaries. Therefore, testing guidelines that govern the use of animals are set both nationally and internationally.

It is very apparent that animal care and use has become vital in animal experimentation for reproducibility and validation of the results and data generated, with these being very prevalent in the Western world, where animal rights organizations abound and are very active and scientists have come under attack by groups who are firmly against the use of animals in research and testing. It is essential that researchers acquire a working knowledge of the procedures and regulations in order to protect themselves and their staff from occupational hazards as well as to protect their labs from criticism or attack from animal rights organizations (Couto, 2011). These situations have generated several legislative processes that are in place to protect research and researchers working with animals. A number of regulatory bodies set guidelines for the care and use of animals in research and testing – such as OLAW, ILAR, AAALAC, USDA – mostly

in the US and Europe. Many other institutions elsewhere follow these and other guidelines in their practices to keep safe.

What is the situation in most developing countries? Are there regulatory infrastructures? Do principal investigators (PIs) observe any protocol reviews before using animals in their research? Are results from animal experiments by PIs from developing countries valid and can they be validated? How can these lapses be managed? This paper is an attempt to define the problems and recommend a pathway for dealing with the situation based on reviews of published reports and discussions from a national workshop.

2 Methods

The research methods used were a comprehensive and systematic review of published reports from developing countries on issues of *adoption of the 3Rs, oversight by an IACUC or/and an ethical committee on animal based research*, the movement towards alternatives to animal use in research on PubMed, as well as focused, face-to-face group discussions led by the author during a one-day national workshop on “IACUC in Nigeria,” organized by the Department of Anatomy, University of Ilorin, Ilorin, Kwara State, Nigeria (July 2011).

Literature search

A comprehensive and systematic search for published reports from developing countries on animal care and use issues was conducted on the PubMed database, without publication date limitation, to determine the quantity emanating. The search strategy used the terms and/or phrases *adoption of the 3Rs, oversight by IACUC or/and an ethical committee on animal based research and alternatives to animal use in research*, refined with the Medical Subject Heading (MeSH) term tool in PubMed, and then combined the search terms using the Boolean operator “AND” with selected developed and developing countries. The search was replicated monthly in May, June, and July 2011, with the same protocol.

Workshop

The Workshop featured a formal opening ceremony chaired by the Deputy Chancellor, Prof. Adeyemi, who represented the Vice Chancellor of the University, Prof. Oloyede, and declared the workshop formally opened. The workshop was chaired by Prof. Ademola Caxton-Martins, Professor of Anatomy and Cell Biology at the University of Ilorin. As the sole facilitator for the workshop, I divided the event into four short sessions of three lectures and a session of small group discussion followed by a reporting session from the groups.

The first lecture centered on the background of the use of animals in teaching, research, and testing and the legislation of different countries, including the US, UK, Canada, Austria, and Australia. The second session focused on IACUCs, what they stand for, their enabling laws, regulations, and guidelines as they function institutionally in the US. The third session dealt with the requirement of IACUCs for consideration and approval of protocols involving the use of animals, with an emphasis on the Three Rs, with examples. The last session divided all par-



ticipants into five groups with specific scenarios as their term of reference. They were to “role-play” as an IACUC committee, based on the information just received, developing and naming the appropriate composition of a typical IACUC to discuss the scenario before them and come up with their decision as an IACUC. A neutral moderator was chosen for each group to discuss the questions of this paper, after which each group presented its reports to the rest of the workshop.

3 Results

The MeSH term tool in PubMed provided alternative search terms to cover the key words used, while the Boolean operator “AND” targeted the country in the address of the corresponding author, which is regarded as the site where the work was done. This was verified by random assessment of the provided addresses on the publications by a blind operator. The developed country with the most published reports on animal research was the United States (Tab. 1). Developing countries with some published reports included India, Taiwan, and Vietnam; there were only two published reports from Sub-Saharan Africa, both from South Africa (Tab. 1).

In all, 262 participants took part in the workshop. Among these were university administrators, deans, professors, senior lecturers, program directors, postgraduate students, laboratory technicians, and undergraduate students from 21 different universities belonging to several disciplines across the country. The workshop lasted 7.5 hours with an hour break.

The focused face-to-face small group discussions summarized current animal care and use for research, education and teaching in developing countries, with particular emphasis on Nigeria, as follows:

- A few cases of functional animal care and use programs exist, but many attempts have failed
- Weak institutional development and access to knowledge in animal welfare management
- Limited and unbalanced capacity to undertake effective training at universities on animals used in research
- Competition and boundaries between countries and institutions limit exchange of knowledge and information
- Lack of, or inadequate, national policies related to animal welfare
- Extensive development of sustainable animal care and use programs at institutions necessary

In many developing countries, there is no legal framework for regulation of animal use in research, education, and testing. National governments need to create an enabling environment for the appropriate use, care, and handling of animals for scientific purposes.

4 Discussion

While a review of literature from a single database might be judged as inadequate to pontificate on the status of publications emanating from developing countries on animal care and use is-

1: Number of published reports on animal welfare issues by selected countries

Search word	“AND” countries	# of published reports obtained
Research Animals	–	2,668,857
Alternatives MeSH terms included:	USA	641,153
Experimentation, Animal	UK	94,406
Animal Research	Canada	107,587
Animal Experimental use	Australia	54,056
Animal Experimental uses	Europe	29,571
Experimental use, Animal	Africa	20,948
Experimental uses, Animal	Asia	25,648
Animal Experiment	South Asia	865
Animal Experiments		
Experiment, Animal		
Experiments, Animal		
Institutional Animal Care and Use Committee	–	775
Alternatives MeSH terms included:	USA	368
Animal Care Committee	Africa	0
Committee, Animal care	Asia	11
Committees, Animal Care	UK	21
Animal Ethics Committee	Australia	10
Animal Ethics Committees	Africa	1
Committee, Animal Ethics	Asia	14
Committees, Animal Ethics	Canada	30
Ethics Committee, Animal		
Ethics Committees, Animal		
IACUC		
IACUCs		
Animal Care and Use Committees		
3Rs	–	247
	USA	48
	UK	29
	Canada	4
	Africa	1
	Asia	5
Alternatives to animal in Research	–	5272
Alternatives MeSH terms included:	USA	1291
Alternative, Animal use	UK	490
Alternatives, Animal use	Europe	479
Animal use Alternative	Asia	74
Use Alternative, Animal	Africa	2
Use Alternatives		



sues, an evaluation of other databases including the Cochrane Library, SCOPUS, CINAHL, EMBASE, as well as Google Scholar, did not retrieve as many published reports as the PubMed database. However, it is noteworthy that there are published reports from developing countries on animal use in research, indicating that animal based experimentation is being conducted. However publications on issues that concern the welfare of the animals used in research are almost nonexistent. The only reports from Africa were both from South Africa, including a review paper by Nyika (2009) discussing the growing phenomenon of animal research being exported to developing countries to circumnavigate the legal protection placed on animals in Western countries, which is a result of the lack of legal framework for regulation of animals used in research, education, and testing in developing countries. The second report, by Southern et al. (1996), considers steps towards the development of a replacement *in vitro* test for quantification of antibodies to tetanus toxin during potency testing of vaccines.

The small group workshop discussions were most interesting for the participants. They readily agreed that there was a need to do something concrete about institutions using animals in Nigeria with no regulations and guidelines, despite associated difficulties that will be encountered in the process. Unfortunately, many countries in the developing world do not have, or do not enforce, such stringent regulations, which is strongly in agreement with the opinion of the workshop participants. While animal welfare research is intended to benefit animals, the fact that legal protection is not in place or is not enforced does not mean that researchers and clinicians should not apply the same rigor to their own study designs. Factors to consider include the impact of the research on the animal versus the potential benefit. Ensuring an experimental design which has fully considered the 3Rs in relation to animals used means using good statistical analysis to ensure the minimum number of animals possible is involved in invasive studies and pre-identifying endpoints for procedures, e.g., limiting venipuncture to two attempts only (Nyika, 2009).

Most national oversight mechanisms emphasize basic principles of humane science, in particular the 3Rs (Russell and Burch, 1959). However, the oversight of animal care and use occurs through a wide variety of local, national, and international mechanisms, some based on legislation (e.g., the European Union) (ESF, 2001), others on peer review or other forms of non-legislated oversight (Canada), and yet others on a combination of legislated and non-legislated oversight (e.g., the United States, New Zealand) (Mellor and Bayvel, 2008). However, science being universal and global (Demers et al., 2006), the results and data generated from any scientific endeavor involving the care and use of animals ought to be valid and reproducible, irrespective of whether it is from a developed or developing country. The mechanism necessary to ensure this, in relation to the care and use of animals for scientific purposes, must be defined, regulated, and structured – even in developing countries.

4.1 Recommendations on development of guidelines for animal care and use for scientific purposes in developing countries

To address the problems of animal welfare in developing countries, it would be inappropriate to adopt international standards

implemented in developed countries. Each developing country should evolve its own standards based on its individual priorities (Rahman et al., 2005). It has been shown that animal welfare improves developing countries' trade opportunities (RSPCA International, 2010). Studies published by the OIE have shown the potential for trade in welfare-assured products from developing countries (Bowles et al., 2005; Huertas Canén et al., 2005).

This paper identifies three types of support tools necessary for an effective delivery system:

- *Technical support tools*, including the promotion of traditional groups and training initiatives. For example, in Nigeria, this author facilitated a national workshop for scientists, students and lab technicians and has encouraged the establishment of associations that bring together interests in animal care and use.
- *Financial support tools*, including research grants and institutional collaboration in animal welfare studies and in developing standard animal holding facilities.
- *Policy-based support tools*, which involve liaison with national governments to encourage the introduction of enabling legislation for institutions involved in animal care and use.

The bottom-line approach for anyone concerned about animal care and use in developing countries is to initiate and encourage an attitudinal/behavioral change of the society regarding animal welfare, based on empirical facts in the context of the values of the society involved. In general, the following recommendations would be helpful to most developing countries and their implementation will be easier and more practical than those designed for developed countries.

4.2 Lessons from the Workshop

The workshop was organized at the national level in Nigeria and concluded with notes to:

- 1) Raise awareness about issues involving animal care and use in Nigeria through universities and research institutes and subsequently to commence a process that will enhance the legislation of the necessary laws through the Nigerian University Commission.
- 2) Develop and sustain a network of all workshop participants for the ease of information dissemination and consideration for advanced courses on animal care and use.

In addition, the workshop also indicated the need for continued education and training of more persons involved with animal care and use, as well as for advanced courses, workshops, and seminars. These can be repeated to accommodate more persons, while it can be expanded as a project to regional levels with the objective of strengthening subject knowledge, as well as teaching and communication skills, of scientists and researchers involved in teaching and supervising graduate students in animal care and use for research, education and training in developing countries. The ultimate objective is contributing to the development of a critical mass of highly skilled and informed persons that will eventually snowball into sustainable capacity building in several developing countries. This can be by "Training the trainers" courses, which would select scientists (university teachers and researchers) responsible for research and training of animal care and use in research to students at undergraduate,



graduate, and postgraduate levels in developing countries. With the improved knowledge, awareness, and skills acquired, they can then reach out to a larger number of students and colleagues in their home institutions.

5 Conclusion

Developing countries need to be cognizant of world trends for the improvement of laboratory animal welfare. Animal ethical review in developing countries would benefit from experiences in Western countries in their evolution toward high standards of experimental animal ethics. Ultimately, the efforts need to bring about an attitudinal change in developing countries by all stakeholders. These role players at all levels should be identified and approached in a language understandable to each and supported by hands-on training in alternative methods. Education through formal curricula is the long-term approach to changing attitudes in the next generation of policy and decision makers. Ultimately, responsibility in this regards rests with them.

References

- Baumans, V. (2004). Use of animals in experimental research: an ethical dilemma? *Gene Ther.* 11, S64-S66.
- Blokhuis, H. J. (2004). Recent developments in European and international welfare regulations. *Worlds Poultr. Sci. J.* 60, 469-477.
- Bowles, D., Paskin, R., Gutiérrez, M., and Kasterine, A. (2005). Animal welfare and developing countries: opportunities for trade in high-welfare products from developing countries *Rev. Sci. Tech.* 24, 783-790.
- Brückner, G. K. (2004). Working towards compliance with international standards. *Rev. Sci. Tech.* 23, 95-107.
- Conlee, K. M. (2008). Chimpanzees in research and testing worldwide: Overview, oversight and applicable laws, *ALTEX* 14, 111-118.
- Couto, M. (2011). Laboratory guidelines for animal care. *Methods Mol. Biol.* 770, 579-599.
- Demers, G., Griffin, G., De Vroey, G., et al. (2006). Harmonization of animal care and use guidance. *Science* 312, 700-701.
- Di Fabio, J. L., Jaramillo, M. T., and Arciniega, J. L. (2002). Adoption of three Rs alternatives for regulatory testing of vaccines in the developing world: possibilities and barriers. *Dev. Biol.* 111, 195-198.
- ESF – European Science Foundation (2001). *Use of Animals in Research* (2nd edition). Strasbourg, France: ESF Policy Briefing. www.esf.org → publication → ESPB15.pdf
- Gruber, F. P. and Hartung, T. (2004). Alternatives to animal experimentation in basic research. *ALTEX* 21, 3-31.
- Hong, H. A. and Hendriks, J. (1999). The use of alternatives to animal tests in developing countries. *Dev. Biol. Stand.* 101, 209-214.
- Huertas Canén, S. M., Cesar, D., and Gil, A. D. (2005). Good management practices in beef cattle production in Uruguay. Training and extension. *ISAH* 1, 264-266.
- Kilkenny, C., Browne, W. J., Cuthill, I. C., et al. (2010). Improving bioscience research reporting: The ARRIVE Guidelines for reporting animal research. *PLoS Biol.* 8, e1000412.
- MacCallum, C. J. (2010). Reporting animal studies: Good science and a duty of care. *PLoS Biol.* 8, e1000413.
- Mellor, D. J. and Bayvel, A. C. D. (2008). New Zealand's inclusive science-based system for setting animal welfare standards. *Appl. Anim. Behav. Sci.* 113, 313-329.
- Nuffield Council on Bioethics (2005). *The ethics of research involving animals* (7). London: Nuffield Council on Bioethics.
- Nyika, A. (2009). Animal research ethics in Africa: An overview. *Acta Tropica* 112S, S48-52.
- Ormandy, E. H., Schuppli, C. A., and Weary, D. M. (2009). Worldwide trends in the use of animals in research: the contribution of genetically-modified animal models. *ATLA* 37, 63-68.
- Rahman, S. A., Walker, L., and Ricketts, W. (2005). Global perspectives on animal welfare: Asia, the Far East, and Oceania. *Rev. Sci. Tech.* 24, 597-612.
- RSPCA International (2010). Animal and people. <http://www.rspca.org.uk/in-action/international/campaignsandissues/developmentandresearch> (accessed 08.08.2011).
- Russell, W. M. S. and Burch, R. L. (1959). *The principles of humane experimental technique*. London: Methuen. Reprinted 1992, Wheathampstead, UK: Universities Federation for Animal Welfare.
- Southern, J., Clements, H., and Spenceley, L. (1996). Steps towards the development of a replacement in vitro test for quantification of antibodies to tetanus toxin during potency testing of vaccine. *Dev. Biol. Stand.* 86, 343.
- Takahashi-Omoe, H. and Omoe, K. (2007). Animal experimentation in Japan: regulatory processes and application for microbiological studies. *Comp. Immunol. Microbiol. Infect. Dis.* 30, 225-246.
- Taylor, K., Gordon, N., Langley, G., and Higgins, W. (2008). Estimates for worldwide laboratory animal use in 2005. *ATLA* 36, 327-342.
- Taylor, K. (2010). Reporting the implementation of the Three Rs in European primate and mouse research papers: are we making progress? *ATLA* 38, 495-517.
- van der Laan, J. W., Brightwell, J., McAnulty, P., et al. (2010). Regulatory acceptability of the minipig in the development of pharmaceuticals, chemicals and other products. *J. Pharmacol. Toxicol. Methods* 62, 184-195.

Correspondence to

Francis A. Fakoya, MD, PhD
Department of Anatomical Sciences
School of Medicine
St. George's University
St. George's, GRENADA, West Indies
Phone: +1473 534 9960
Fax: +1473 444 1602
e-mail: ffakoya@sgu.edu