

# International reflections: looking back over the last 20 years

## Dr Judy A. MacArthur Clark

Animals in Science Regulation Unit  
Home Office  
London SW1P 4DF, United Kingdom

## Introduction

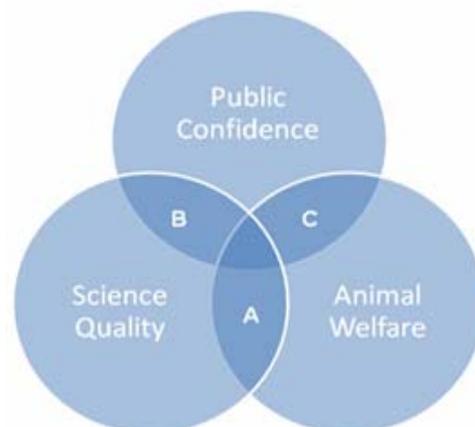
My career in laboratory animal science started almost 40 years ago when, as a young veterinary graduate, I took a research position with the Universities Federation for Animal Welfare (UFAW: [www.ufaw.org.uk](http://www.ufaw.org.uk)). Thus I was introduced to the already emerging role for veterinarians in this field and I encountered the concept of alternatives in the shape of UFAW's "3Rs" (Replacement, Reduction and Refinement). Nevertheless, the greatest progress in this field has undoubtedly been made over the last 20 years.

A guiding principle which I believe has influenced ethical regulation over this 20-year period is the "Regulatory Balance" which can be represented as three overlapping circles (Figure 1, MacArthur Clark 2011). Regulators must provide balance between the needs of science and the needs of animals. Any regulatory system must ensure that bureaucracy and rules do not become too burdensome so as to inhibit scientists from being able to address important research questions. But equally important is that animals must not suffer unnecessarily. Furthermore, there is strong evidence to show that good animal welfare delivers good science (the overlapping area A).

It is this balance between science and welfare which provides the public with confidence in the regulatory system. The public wants to benefit from scientific advances, but also wants to be reassured that animals

are not suffering unnecessarily (the overlapping areas B & C). The nature of this balance will differ between countries taking into consideration diverse cultural, economic, religious and social factors. However, the guiding principle of the Regulatory Balance should always be applied in determining the right approach to research animal use.

This simple concept can, in my experience, be used to determine the direction which regulations should take. The spectrum of diverse interests in this field, ranging from animal protectionists to scientific researchers, often argues for conflicting outcomes in debates, and any attempts to pander to one sector to the detriment of the others is rarely successful. This paper considers each of the elements of this Regulatory Balance and how they have been applied internationally over the last 20 years.



**Fig. 1** The Regulatory Balance: a hypothetical structure for regulating the use of animals in research (MacArthur Clark 2011).

## Changes in science

A number of significant changes in science impact on how we need to consider experiments on animals. Perhaps foremost of these is the growth of genetic modification, especially in mice. According to UK statistics, in 1995, 2.7 million animals were used in scientific procedures of which about 15% were genetically altered. By 2010, the total had increased to 3.6 million of which over 50% were genetically altered (Home Office 2011). This genetic revolution, combined with our ability to carry out research on an ever smaller scale (e.g., analytical sample size, surgical approaches, implantable devices), has enabled studies which would not have been possible in the past.

At the same time, we have seen changing disease demographics. Many therapies for acute diseases have now been discovered and we see an increase in chronic and rarer conditions, e.g., diseases of ageing, mental illness, genetic and metabolic conditions, together with a return of serious bacterial conditions which we once thought antibiotics had eliminated. Through our ability to compare detailed genetic and other characteristics, we are also learning that many traditional animal models are not as relevant to the human condition as we have believed. Furthermore, the use of stem cells in regenerative and other therapies, and the development of animals containing human material, both raise new ethical questions for the scientific community (Academy of Medical Sciences 2011).

In the field of regulatory safety testing, our ambition to reduce the numbers of animals used is often in conflict with a trend to reduce any risk to humans and the environment. This is helpfully stimulating a new approach to toxicity testing, elegantly described in the report "Toxicity testing in the 21<sup>st</sup> Century" (Institute of Medicine 2007), together with an improved environment for data-sharing among pharmaceutical companies.

## Issues affecting animal welfare

In 1959 William Russell and Rex Burch, working on a project proposed and sponsored by UFAW, published their *Principles of Humane Experimental Technique* (Russell & Burch 1959) but a number of years had to pass before their concept of the 3Rs became part of our common thinking.

The Fund for the Replacement of Animals in Medical Experimentation (FRAME) was founded in the UK in 1969 but further progress was slow. The Center for Alternatives to Animal Testing (CAAT) was founded at Johns Hopkins University in the USA in 1981 and the European Centre for the Validation of Alternative Methods (ECVAM) was established by the European Commission in 1992. By the early nineties there were international moves to promote alternatives; the first World Congress on Alternatives and Animal Use in the Life Sciences was held in Baltimore in the USA in 1993.

Most of the attention so far has been directed towards validating replacement alternatives in regulatory testing yet progress has arguably been disappointing. Given that about 75% of animals are used in non-regulatory areas of basic and applied research, one might ask whether a greater focus in these areas would be more beneficial. This has been an aim of the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs: [www.nc3rs.org.uk](http://www.nc3rs.org.uk)) founded in the UK in 2004 following a recommendation of a Select Committee of the House of Lords (House of Lords 2002). At a European level, the new Directive (2010/63/EU) places the 3Rs at the centre of its aims, significantly both in basic sciences and in regulatory testing (European Parliament 2010).

Many feel that the opportunities for progress in refinement have been undervalued. The general acceptance that refinement includes enrichment of an animal's environment to satisfy its behavioural needs has led to this becoming standard practice for all species in many laboratories. A further notable development in 2010 was the UK Coalition Government pledge to work to reduce the use of animals in research (HM Government 2010). This will be a science-led initiative which pays attention to refinement opportunities as well as reduction and replacement.

Another remarkable change over the last 20 years has been the growth of specialist expertise in this field among veterinarians. While the American College of Laboratory Animal Medicine (ACLAM) was founded as early as 1957, we waited until the 1990s for Japan (JCLAM) and Europe (ECLAM) to follow suit. In 2005, the Korean College (KCLAM) was formed and an International Association of Colleges of

Laboratory Animal Medicine (IACLAM) was created with these four colleges as the founding members (MacArthur Clark 2008).

The focus of IACLAM has been to promote education and certification of veterinary specialists and to ensure effective dissemination of relevant information. Increasingly veterinarians have been recognised in national and regional legislation with the roles of Attending Veterinarian (USA) (Animal Welfare Act 1985a), Named Veterinary Surgeon (UK) (RCVS 2004) and Designated Veterinarian (Europe) (European Parliament 2010). Veterinarians advise on the care and welfare of research animals and play an important role in ethical review. In 2011 IACLAM partnered with the World Organisation for Animal Health (OIE: [www.oie.int](http://www.oie.int)) and the Institute for Laboratory Animal Research (ILAR: <http://dels.nas.edu/ilar>) to publish guidance which will have international impact on the training of laboratory animal veterinarians (Bayne et al. 2011).

Raising scientific and welfare standards internationally has been a significant feature of many organisations in recent years. Whilst ILAR was founded in 1953 within the US National Academies of Science, it was not until the early 2000s that ILAR created an International Committee which now is leading the development of an International Primate Plan. Likewise, ICLAS (International Council for Laboratory Animal Science: [www.iclas.org](http://www.iclas.org)) was founded in 1956 and today is working with CIOMS (Committee of International Organisations of Medical Sciences: [www.cioms.ch](http://www.cioms.ch)) to update the international guiding principles for animal research (CIOMS-ICLAS 2011). AAALAC (American Association for the Accreditation of Laboratory Animal Care: [www.aaalac.org](http://www.aaalac.org)) was founded as a US organisation in 1965 but in 1996 recognised its international role and changed its name (Association for Assessment and Accreditation of Laboratory Animal Care) to reflect its wider remit.

The CCAC (Canadian Council on Animal Care: [www.ccac.ca](http://www.ccac.ca)) was created in 1968 and, in 2011, hosted the 8<sup>th</sup> World Congress on Alternatives and Animal Use in the Life Sciences (WC8) in Montreal, a major international undertaking. The OIE has 178 member countries and in 2010 published a chapter in its Terrestrial Animal Health Code setting standards for the use of animals in research and education (OIE 2010). This has the potential to significantly affect

regulatory systems globally, especially in developing countries which are emerging scientifically.

All these initiatives are directed towards improving the welfare of research animals globally whilst balancing these improvements with the expanding demands of science. But perhaps one of the most significant developments in the last 20 years has been the growth of ethical review of research proposals. In the mid 1980s, new legislation was implemented in both the USA (Animal Welfare Act 1985b), and the UK (Animals (Scientific Procedures) Act 1986) which introduced this concept. The aim was to engage others outside the immediate research team in evaluating scientific proposals and determining what should be done and at what cost to the animals. This is usually referred to as a cost (harm)-benefit assessment and involves input from veterinarians and animal care staff as well as scientists and those who represent broader public opinion. Directive 2010/63/EU implements this cost-benefit assessment as an element of project authorisation in all 27 member states of the European Union from January 2013.

## Changes in public confidence

In 2006 the organisation Pro-Test ([www.pro-test.org.uk](http://www.pro-test.org.uk)) was started following an anti-vivisection rally in Oxford, UK attended by 16-year-old student, Laurie Pycroft. Pro-Test has helped change the attitudes of the public, politicians and media towards animal research.

Between 1999 and 2010, Ipsos-MORI has carried out regular surveys of UK public opinion about animal research (Ipsos MORI 2010). These surveys show that conditional acceptance of animal research has remained fairly constant at about 88% provided that the research is for medical purposes, causes no unnecessary suffering and that no alternative exists. Moreover, unconditional acceptance has almost doubled over the same period from 32% to 60%.

These results suggest that the UK public tends to support the need for a balance between science and welfare. There is a sophisticated understanding that science using animals needs to be regulated but also empowered to make its effective and necessary contribution to society. The public believes that animals should not suffer unnecessarily for these benefits and seeks to have confidence and reassurance that this is the case.

## Conclusion

It is clear that the last 20-year period has demonstrated the importance of the “Regulatory Balance” in realising an environment of successful research which cares for animals and attracts public support. Throughout the world, and within the full range of cultural, economic, social and religious influences, we might ignore this balance at our peril.

## References

- Academy of Medical Sciences 2011: Animals containing human material. Available electronically at <http://www.acmedsci.ac.uk/p47prid77.html>.
- Animal Welfare Act 1985a: Improved standards for laboratory animals, USA. Responsibilities and Functions of Attending Veterinarians. Available electronically at <http://www.nal.usda.gov/awic/pubs/Legislat/awabrief.shtml#Q1>.
- Animal Welfare Act 1985b: Improved standards for laboratory animals. Available electronically at [http://awic.nal.usda.gov/nal\\_display/index.php?info\\_center=3%20&tax\\_level=4&tax\\_subject=182&topic\\_id=1118&level3\\_id=6735&level4\\_id=11095&level5\\_id=0&placement\\_default=0](http://awic.nal.usda.gov/nal_display/index.php?info_center=3%20&tax_level=4&tax_subject=182&topic_id=1118&level3_id=6735&level4_id=11095&level5_id=0&placement_default=0).
- Animals (Scientific Procedures) Act 1986: Available electronically at <http://tna.europarchive.org/20100413151426/http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm>.
- Bayne, K.; Bayvel, D.; MacArthur Clark, J.; Demers, G.; Joubert, C.; Kurosawa, T.; Ouajdi, S.; Rivera, E.; Turner, P. 2011: Harmonizing veterinary training and qualifications in laboratory animal medicine: a global perspective. *ILAR Journal* (in press).
- CIOMS – ICLAS 2011: Draft revision of International Guiding Principles for Biomedical Research Involving Animals. <http://ora.msu.edu/ICLAS/index.html>.
- European Parliament 2010: Directive 2010/63 on the protection of animals used for scientific purposes. Available electronically at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:EN:PDF>.
- HM Government 2010: The Coalition: our programme for government, page 18. Available electronically at [http://www.cabinetoffice.gov.uk/sites/default/files/resources/coalition\\_programme\\_for\\_government.pdf](http://www.cabinetoffice.gov.uk/sites/default/files/resources/coalition_programme_for_government.pdf).
- Home Office 2011: Statistics on scientific procedures on living animals in Great Britain 2010. Available electronically at <http://www.homeoffice.gov.uk/publications/science-research-statistics/research-statistics/science-research/spanimals10/spanimals10?view=Binary>.
- House of Lords 2002: Select Committee Report on Animals in Scientific Procedures. Available electronically at <http://www.publications.parliament.uk/pa/Id200102/Idselect/Idanimal/150/150.pdf>.
- Institute of Medicine 2007: Toxicity testing in the 21<sup>st</sup> Century: a vision and a strategy. Available electronically at [http://www.nap.edu/openbook.php?record\\_id=11970&page=1](http://www.nap.edu/openbook.php?record_id=11970&page=1).
- Ipsos MORI 2010: Views on Animal Experimentation. Available electronically at [http://www.ipsos-mori.com/DownloadPublication/1343\\_sri-views-on-animal-experimentation-2010.pdf](http://www.ipsos-mori.com/DownloadPublication/1343_sri-views-on-animal-experimentation-2010.pdf).
- MacArthur Clark, J. A. 2008: IACLAM: A global vision for laboratory animal medicine. *Proceedings of the 6<sup>th</sup> World Congress on Alternatives & Animal Use in the Life Sciences, Tokyo, Japan. AATEX 14, Special Issue. 735-737.* <http://altweb.jhsph.edu/bin/k/g/paper735.pdf>.
- MacArthur Clark, J. A. 2011: International developments relating to the use of animals in science. *Proceedings of the 5<sup>th</sup> Pan-Commonwealth Conference, Accra, Ghana* (in press).
- OIE 2010: Use of animals in research and education. Chapter 7.8, OIE Terrestrial Animal Health Code. OIE, Paris. [http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre\\_1.7.8.htm](http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.7.8.htm).
- RCVS 2004: Guidance for named veterinary surgeons employed in scientific procedure establishments and breeding and supplying establishments under the Animals (Scientific Procedures) Act 1986. Available electronically at <http://www.rcvs.org.uk/advice-and-guidance/guide-to-professional-conducts-for-veterinary-surgeons/k-nvs-guidance/>.
- Russell, W. M. S.; Burch, R. L. 1959: Principles of humane experimental technique (UFAW). Available electronically at [http://altweb.jhsph.edu/pubs/books/humane\\_exp/het-toc](http://altweb.jhsph.edu/pubs/books/humane_exp/het-toc).