



Workshop 3.2

Establishing the 3Rs principle around the world

Establishing the Three Rs Principle: A Plea for an International Severity Standard

Andrzej Elzanowski
Poland

Summary

Severity (harm, invasiveness) scales focus the attention of both regulators and researchers on highly invasive experiments and thus help to promote the 3Rs, especially the refinement. A severity scale is critical to the quality of ethical review processes (ERPs) in limiting arbitrariness and situational opportunism of assessments, defining the acceptability ranges for some animal uses, especially in education, and differentiating justification requirements. An international severity scale would improve ERPs in some countries and put pressure on others to institute them. An international severity scale would also facilitate the promulgation of other international requirements and restrictions that are applicable only within appropriate severity grades and that otherwise would be impractical, questionable or vague. I therefore advocate finding an appropriate international organisation to negotiate and propose an international severity standard and to launch an international campaign to promote its acceptance.

Keywords: animal welfare, international standards, animal research ethics, harm/pain/severity scale, refinement

Introduction

With many countries worldwide having little if any regulations of animal research and testing, any reasonable *minimum* standard adopted by an international committee is better than none, both in terms of its immediate effects when used by animal advocates, and as a draft for future improvements. The emphasis on the minimum is because any international standardisation initiative must not contravene more elaborate or restrictive standards already adopted by some progressive countries. However, in opposition to the widespread uncritical deference to religion and cultural diversity, the universal ethics of respecting all sentient beings may and should override any tradition of animal abuse.

There are at least five domains of standards that are jointly necessary to establish the 3Rs throughout the World: procedures (experimental and veterinary), housing and transport, ethical assessment and review, education and training, and enforcement. Only the two of them, the experimental and the housing and transport domains, have so far attracted considerable attention

and effort. The only official world standards, for euthanasia and humane endpoints (International Council for Laboratory Animal Science, see www.iclas.org/) are in the procedural domain, and both are special cases insofar as both are concerned with death, which is an ultimately invasive procedure but can, if an appropriate care is taken, be administered quickly with only momentary or no suffering.

Animal research encompasses procedures ranging from non-invasive and *prima facie* benign procedures (such as handling, weighing, taking urine samples) to procedures inflicting extreme suffering and/or death. All animal research should be subject to ethical review and regulated, because even essentially harmless procedures can be harmful if improperly performed (Orlans, 1993), which is particularly true of wildlife research. On the other hand, one must not apply the same restrictions and requirements to, say nutritional experiments and neurosurgical procedures, because this would needlessly hamper science, antagonise research community, and ultimately backfire at all ethical oversight and legal control of animal research. In the



long run, over-regulation is known to be counterproductive for complex, intellectually demanding activities and this is certainly true of scientific research.

For that reason, among dozens of standards that are missing and necessary for the implementation of 3Rs, I advocate giving the top priority to the development of an international severity scale because it is badly needed as a yardstick for calibration of many other standards which turn out to be severity-sensitive. A severity scale is a conceptual tool for extending ethical oversight to all research on and with animals but without unduly hampering it. It is also needed to improve ethical review processes (ERPs) in some countries, especially in the US, and to have them started in others (especially in Russia and China).

A severity scale has another, psychological and thus evasive but potentially powerful educational effect on researchers if they have to assess and thus to confront themselves the harm they intend to do to their animal subjects. For example, the current Polish application forms require the researchers to determine the severity grade first, but a local ethics committee may correct the rating (in a special field). As a result, the researchers' rating is usually correct, which contrasts with the common practice of underrating the severity of one's own experiments (Orlans, 1993).

The importance of severity scales for ethical review processes

The current ideal for the ethical evaluation of animal research is best represented by Bateson's cube (Bateson, 1986) with its three variables, quality of research, medical benefit, and animal suffering, which all determine the ethical acceptability of a research project. It reflects the present western compromise between the majority of research community that conveniently embraces the anthropocentric dogma (Porter, 1992), and moral concerns of general public, supported and authenticated by the majority of lay philosophers. The ensuing compromise deserves the label of controlled speciecism: animals are harmed and killed in the name of substantial human benefits but at least animal suffering (and, to a various degree, life itself) should be reckoned with and not dispensed for trivial or questionable purposes. In reality, the control of speciecism varies between countries and animal species, and the Bateson's cube, which contains a space that is forbidden despite highest research quality and benefits, represents an ideal that may be approached only by a few nations and only with respect to primates, cats, and dogs.

In order to be operational, the Bateson's cube requires a scale or calibration for each of the three variables. Unfortunately, a precise quantitative scale does not seem possible for any of the three variables and the only way make them comparable is to agree on their gradation. It is highly desirable to have a graded classification for each of the variables (Porter, 1992) especially because an average human committee, with a majority of members with vested interests in continuing animal research, tends to overestimate human benefits and to underestimate non-human harms.

For the sake of implementing 3Rs, it is, therefore, essential to have the experimental procedures categorised by their severity

grade prior to the evaluation of any invasive experiment. The gross underestimations of animal harms stem not only from largely unarticulated speciecism, but also from situational opportunism of assessments, with cronyism as a major but not the only factor. Situational opportunism stems from the pervasive net of personal, professional, and administrative interdependencies between the members of ethics committee as well as their ties with the outside colleagues who apply for approval of their projects. In Poland, we managed to keep, so far, our local ethics committees inter-institutional, with representatives from several independent research organisations, which reduces, but by far not eliminates, the impact of situational opportunism (which I can attest as a member of a local ethics committee).

While it is essential to make sure that even non-invasive handling of animals is done properly by responsible individuals, and thus to subject all animal research to ERP (which is the case in some countries including Poland), it would be counterproductive to require the same levels of justification for non-invasive or only slightly invasive procedures (such as blood sampling) as for heavy survival surgeries or acute toxicity testing. I therefore propose, as a rule for the ERPs, that requirements of project justification be severity-sensitive. This rule is implemented in the application forms established by Poland's National Ethics Committee, which require addressing clinical applications and documenting database searches only for two highest severity levels.

The use of live vertebrates in education is notoriously contentious, as exemplified by the admitted failure of the (really hard!) Working of Party of the Institute of Medical Ethics (UK) to reach consensus with regard to "invasive uses of animals" in undergraduate teaching (Smith and Boyd, 1991). This difficulty could be largely resolved if the use of animals could be limited to well-defined levels of severity although some disagreement as to the assessment of educational benefits will probably persist. Poland's first National Ethics Committee ruled in 1999 that only the lowest severity grade is acceptable for educational and training purposes and the rule seems to have been generally respected (except for a few objections from veterinary schools).

Severity grades as qualifiers of procedural standards

The harm scales permit to calibrate all restrictions and requirements to the harm to be inflicted by generic procedures, and thus to sensibly regulate all animal use in research, testing and education. Hence the enormous importance of a severity scale as a superstandard for some procedural standards that cannot be sensibly proposed without using severity grades as qualifiers. Without attempting a comprehensive review of all procedural standards that are missing for the effective implementation of 3Rs, the following examples suffice to demonstrate the significance of having an international severity scale as a superstandard for making research restrictions commensurate with the expected harms.

Among many missing international standards are those defining the extent of veterinary supervision of experiments and the limits to repeated use of animal subjects. Both can be sensibly



proposed only with reference of severity grades inasmuch as requiring veterinary supervision for, or forbidding a repetition of some least invasive procedures would be impracticable and sometimes absurd.

Largely neglected are any regulations of wildlife research, although trapping and other more or less invasive experimental methods have been widely used for several decades (Cuthill, 1991) and the current widely used radio-tracking techniques (Mech and Barber, 2002) raise most serious concerns. The Canadian Council on Animal Care (CCAC) is the first major national agency that thoroughly addressed this issue (Griffin and Gauthier, 2004). Wildlife research regulations should be conceived as highly severity-sensitive because their enforcement in the field heavily depends of the levels of acceptance by the specific community of field naturalists and conservationists.

An outlook on national severity standards

Worldwide, a severity (harm, invasiveness) scale has by now been adopted by at least nine countries (tab. 1) including most Western countries leading in research.

Several different approaches to defining severity scales (tab.1) have been reviewed by Orlans (2000b) and Purves (2000). The latter mistook the Swiss standard for the retrospective assessment of severity (Bundesamt für Veterinärwesen, 1994b) for the German scale and listed the classification of animal experiments by Australia's National Health and Medical Research Council (NHMRC) among pain and distress classification systems although it cannot be regarded as such. The Australian classification is based on a mix of two criteria: kind of experimental procedure and some of its qualitative consequences for animal welfare. The Australian classification may be useful for devising a severity scale but cannot be used as such because it does not

define any pain and distress grades or levels across various kinds of procedures, which is what a severity scale is about. It is regrettable that Australia did not adopt the excellent standard developed by the Australian and New Zealand Council for the Care of Animals in Research and Teaching (Mellor and Reid, 1994).

The majority of five countries, including New Zealand, Switzerland, Germany, Poland, and Sweden, use a ternary scale, that is, categorise all acceptable invasive procedures into three severity grades. The Netherlands used to have a ternary scale since 1979 (Orlans 1996); this scale is said to be currently revised. Two countries, Canada and UK, use a quaternary severity scale, that is, categorise all acceptable invasive procedures into four severity grades. In addition to 3 or 4 basic levels, some countries recognise a zero level for non-invasive or painless (which does not mean harmless) procedures and some countries identify extreme and/or unacceptable procedures in a special category (X in tab. 1).

The categorisation of animal experiments used by the US Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) was designed in the 1970's (Orlans 1993, 2000b) as a catch-all formula for reporting rather than ethical review purposes. It is not really a severity scale (hence it is not listed in tab. 1) as it is based on the use or non-use of anaesthesia (as deemed appropriate for various reasons) rather than severity *per se*. Three categories of experiments are defined in the column headings in the Annual Report of Research Facility form (USDA/APHIS, 1991): experiments involving no pain, distress or (sic) use of pain-relieving drugs (column C), experiments involving pain or distress which are alleviated by anaesthetics, analgesics or tranquilizers (column D), and experiments for which administering such drugs for relief "would have adversely affected the procedures, results or interpretation of the teaching, research, experiments, surgery or tests" (column

Tab. 1: Severity scales worldwide. 0 denotes non-invasive procedures on living animals. X denotes extreme or unacceptable procedures if recognised as such in the cited national standard.

Country	Severity grades	Since	Source
The Netherlands	under revision ¹	1979	Orlans (1996)
Finland	2	1985	Laboratory Animal Act (1076/1985)
Canada	4 ²	1987	CCAC (1991)
New Zealand	0+3+X ³	1988	Mellor and Reid (1994)
Switzerland	0+3	1994	Bundesamt für Veterinärwesen (1994a)
Poland	0+3+X	2000	Krajowa Komisja Etyczna (1999)
UK	4+X	2000	Home Office (2000)
Germany	0+3 ⁴	2000	Bundesministerium der Justiz (2000)
Sweden	3 ⁵	2001	Djur Skydds Myndigheten (2001)

¹ The Netherlands used to have a three-level severity scale.

² Of the four counted levels (B through E), the lowest (B) includes some procedures categorized elsewhere as 0 and the highest (E) includes some procedures categorized elsewhere as X.

³ Applied in each of the five harm ("welfare compromise") domains (Mellor & Reid, 1994)

⁴ Used in the application form but not explicitly defined; duration of a procedure is considered separate from the severity, as the form requires its specification (1 day, 1-7 days, 7-30 days, and above 30 days) in addition to a severity grade.

⁵ Sweden used a six-level scale in the years 1979-1989.



E). It is only for the latter (column E) category that an approval by an Institutional Animal Care and Use Committee (IACUC) is required. The requirements stated in the Annual Report form are interpreted and elaborated in the APHIS policy, the most recent version of which (USDA/APHIS, 1997) defines a painful procedure as any procedure that can reasonably be expected to cause more than slight or momentary pain". In fact, only the most invasive procedures such as terminal surgery, Freund's complete adjuvant, ocular and skin irritancy testing, extensive irradiation, long-term food or water deprivation, noxious electrical shock, paralysis or immobility are considered to be painful. The majority of experiments is liberally categorised as causing only slight or momentary pain, lumped with non-invasive procedures, and thus effectively ignored. This regulation may have been progressive in the 1970's, i.e., at the time of general callousness toward animal suffering in the US and most other countries, but today it is outdated and inappropriate as a severity standard for use in ERP. It is most deplorable that the US research community has contravened sincere efforts on the part of its progressive minority (as well as USDA in 1987) to establish an adequate severity standard (Orlans, 2000b), which puts the US behind many other Western nations in a key ethical matter.

A two-level severity scale has also been established in Finland by its 1076/1985 Laboratory Animal Law, each level ("class") being defined by several examples in a regulatory act (Decision 477/1986) issued by Finland's Ministry of Agriculture and Forestry, and a grade 0 is also used in the ERP for experiments that "do not cause harm or discomfort" and thus do not require any permits (Kai Pelkonen, pers. comm.).

There are countries in which no severity scale is prescribed by any law or regulation and yet some severity assessment is done in the ERP. For example in Singapore the veterinarian in charge of the care of experimental animals is expected to assess the severity of the projected experiment (Su Hua Leow, pers. comm.) although the elaborate Guidelines on the Care and Use of Animals for Scientific Purposes, as instituted by the National Advisory Committee for Laboratory Animal Research in 2004, do not define a severity scale.

Ternary scales

The most refined ternary scheme has been devised by ANZC-CART to consider pain and distress from all sources which are conceptualised as five domains (Mellor and Reid, 1994) and then to add them in calculating the summary severity grade. This scheme should be used together with the Swiss rating of procedures (see below) by all regulatory bodies and standard setting

panels for assigning examples to each level, but may be too complex for an average local ethics committee.

The Swiss Federal Veterinary Office (Bundesamt für Veterinärwesen, 1994a) distinguishes four expected (pre-experimental) severity grades starting with grade 0 for non-invasive procedures (such as ethological observations). Examples for each grade are provided in 12 areas: restrictions of movement and diet, interference with reproduction and development, sampling and surgery, exposure to physical agents, pharmacology and toxicology, microbiology and parasitology, immunology, analgesia and inflammation, heart and circulation disorders, hormonal and metabolic disorders, neurological and behavioural disorders, and cancer. A separate standard (Bundesamt für Veterinärwesen, 1994b) defines procedures and symptoms for common laboratory species for the retrospective determination of the actual severity grades in ongoing projects. Retrospective review is essential for an effective oversight and has recently been addressed in the European Commission and Britain (LASA, 2004). Unfortunately, the concept is completely unknown in Poland (and probably most other new EU member states) and adds to the long list of missing standards. Retrospective review would also benefit from a severity scale as projects involving the most invasive experiment should obviously be revisited first. This is because ethics committees in many countries may not have enough capacities to conduct retrospective review of all approved projects.

Poland's National Ethics Committee for Animal Experimentation (Krajowa Komisja Etyczna do Spraw Doświadczeń na Zwierzętach), empowered by the 1997 Animal Welfare Act to set up standards for the ERP, adopted in 1999 an essentially ternary scheme (tab. 2) which is based on the scale once proposed for the US by the Scientists' Center for Animal Welfare (Orlans, 1990, see also Fraser, 1990). From the very beginning the scheme has been effectively enforced through application forms, which require the severity grade to be specified by the investigator, and make several requirements dependent upon the severity grade, e.g., only the lowest severity grade is permissible for educational experiments, and clinical implications need to be specified for higher grades. The use of severity grades has been mandated by Poland's new Animal Experimentation Act of January 21, 2005 (Dziennik Ustaw 05.33.289 of 24 February 2005) which requires (in Art. 20) a determination of the severity grade in the permit application and delegates (in Art. 28) the definition of the severity scale to the National Ethics Committee, the latter provision making it inevitably dependent on the political vicissitudes of this body.

Tab. 2: Severity scale instituted by Poland's National Ethics Committee (Krajowa Komisja Etyczna, 1999) and largely based on the scale once proposed by the Scientists' Center for Animal Welfare (Orlans, 1990).

Grade 1	Noninvasive
Grade 2	Light, momentary pain/distress or minor discomfort for a long duration.
Grade 3	Moderate pain or distress.
Grade 4	Acute pain or distress or irreversible physical or psychological impairment.
Grade X	Unacceptable extreme suffering.

The ceding post-communist government has just appointed a new, egregiously inappropriate National Ethics Committee, with an immediate effect of the Scale of Invasiveness having been removed from the Web page of the Ministry of Science.

After the unfortunate abandoning its once pioneering severity scale (Orlans, 2000b), Sweden has now reinstated a simple three-grade scale, with each grade defined by a dozen of known examples by the Swedish Animal Welfare Agency (Djur Skydds Myndigheten, 2001).

Three severity grades are used in Germany's application form for the animal experimentation permit (to a state or *Land* government), which is part of the ordinance issued the Federal Ministry of Justice (Bundesministerium für Justiz, 2000) pursuant to the 1998 update of the German Animal Welfare Act. However, there is no explicit definition of these grades, which are meant to scale only the intensity but not the duration of procedures. The latter has to be specified separately in the same form in terms of days.

The Japanese "Standards relating to the care and management etc. of experimental animals" (issued in 1980 by the Prime Minister's Office) do not contain any provisions for the use of severity scales. However, some institutions voluntarily use the ternary scale devised in the eighties by the US Scientists' Center for Animal Welfare (Yukihisa Matsuda, pers. comm.).

Quaternary scales

The Canadian Council on Animal Care defines five categories of invasiveness (CCAC, 1991). However, the lowest of them refers to those invertebrates that are considered to be non-sentient and to tissue cultures, and thus will be ignored for the purpose of comparisons to other national standards. The lowest of the remaining four grades (B) comprises a mix of procedures that are *per se* non-invasive, such as temporary maintenance of a herd under a production management system to be tested, and clearly invasive procedures such as blood sampling, simple injections or approved methods of euthanasia involving rapid unconsciousness. The label "minor stress or pain of short duration" for the following level C underestimates the severity of at least some of the listed procedures (such as "stressful restraint"). The next level D is again mixed as admitted by its title "moderate to severe distress or discomfort". The top level E includes several procedures that are widely considered unacceptable (such as the use of muscle relaxants and paralytic drugs without anaesthesia or burn infliction on non-anaesthetised animals) as well euthanasia methods not approved by the CCAC. And yet the entire category is not identified as unacceptable (and thus is not identified as grade X in tab. 1). Because of the mixed contents of its categories, the Canadian scale lacks transparency and tends to underestimate, at least verbally, the severity of listed procedures.

In the UK, the Home Office (2000) specifies the four categories in its *Guidance to the Operation of the Act*. The lowest is called "unclassified" and includes terminal experiments entirely under general anaesthesia, and the remaining three are called mild, moderate, and substantial. In addition, "the Secretary of State will not license any procedure likely to cause severe pain or distress that cannot be alleviated [Section 10(2A)].", which is

what is categorised in table 1 as forbidden or extreme procedures (grade X). Thus the British scale seems to be best conceptualised as 4+X (tab. 1) even though classifying terminal anaesthesia in a category of its own seems somewhat inconsistent because there are many procedures that are comparable in severity to anaesthesia, and euthanasia *per se* is not covered by the British scale. This scale is used for an *upper limit* on the severity acceptable for an individual experimental protocol. In addition, there are severity bands for programmes of work where they indicate the *average severity*, taking into account numbers of animals affected, intensity and duration of the adverse effects, for all animals expected to be used during the whole programme.

An evaluative outlook

The great advantage of ternary schemes is that they are simple and nearly self-explanatory: a procedure that is not comparable to either the most or the least invasive examples falls in the middle. Its simplicity also makes it independent of frequent updates and elaborations. There are inevitable complaints about the relative imprecision of a ternary assessment (U. Hansson, pers. comm.), especially in Sweden, where a refined six-level scale was formerly used. However, the refinement of laws should not go too far beyond the possibilities of their enforcement. Therefore, simple ternary scales (similar to the Polish and the current Swedish scale) seem to be the best choice for countries such as new EU member states, with little experience and resources to carry out ERP. A two-level scale, with all experiments categorised as either mild or severe, seems too simplistic as many experiments that cause considerable suffering may fall in the mild(er) category, although a judicious use a two-level scale is probably much better than none.

Whatever the number of severity grades, it is of great importance to have a category for procedures that are harmless by laboratory standards as even the least invasive procedures may turn harmful if improperly executed (as in the case temporary captivity followed by a release at the wrong time or place). This is especially true for wildlife research, which is usually done in the name of nature conservation and thus looks animal-friendly or at least benign to the public. In fact, research on wild animals frequently leads to slow and painful death, e.g., when caused by a too tight telemetric collar, which is on the average worse than death from most natural causes.

A plea to speed up international standardisation of severity scales

In view of the urgent needs and considerable number of good regional standards, the process of turning them into World standards needs to be substantially accelerated. Each of the five categories of needed standards requires different expertise and philosophical perspective, calling for involving more organisations in the process, but there may be not enough of them to do the job. For example, while the ICLAS and other laboratory animal associations are well prepared to propose experimental standards and the housing and transport standards, the three other domains should be tackled by bodies representing broader



expertise including appropriate psychological and philosophical perspectives. One of several candidate organisations (Purves, 2000) is the International Organization for Standardization (ISO) which is currently embarking on social responsibility issues (Frost, R., 2005. ISO Press Release 947: <http://www.iso.iso/en/commcentre/pressreleases/>) and thus could be approached to support the development of a standard severity scale as a good exercise in applying public responsibility in science and biotechnology.

References

- Bateson, P. (1986). When to experiment on animals. *New Scientist* 109, 30-32.
- Bundesamt für Veterinärwesen (1994a). Einteilung von Tierversuchen nach Schweregraden vor Versuchsbeginn (Belastungskategorien). Allgemeine Leitsätze und Beispiele zur analogen Klassierung weiterer Versuche. Bundesamt für Veterinärwesen, Information Tierschutz 1.04.
- Bundesamt für Veterinärwesen (1994b). Retrospektive Einteilung von Tierversuchen nach Schweregraden (Belastungskategorien). Bundesamt für Veterinärwesen, Information Tierschutz 1.05.
- Bundesministerium der Justiz (2000). Allgemeine Verwaltungsvorschrift zur Durchführung des Tierschutzgesetzes. *Bundesanzeiger* 52 (36a): 1-16.
- CCAC (1991). Position Statement: Categories of Invasiveness in Animal Experiments. Ottawa, Canadian Council on Animal Care. (Reprinted in Olfert, E. D., Cross, B. M., and McWilliam A. A., eds. *Guide to the Care and Use of Experimental Animals Vol. 1*, 2nd ed., 1993).
- Cuthill, I. (1991). Field experiments in animal behaviour: methods and ethics. *Animal Behaviour* 42, 1007-1014.
- Djur Skydds Myndigheten (2001). Etisk prövning av djurförsök. Vägledning till ansökan.
- Fraser, A. F. (1990). An analysis of suffering. In B. E. Rollin & M. L. Kessel (eds.), *The Experimental Animal in Biomedical Research*, Vol. 1. Boca Raton, CRC Press.
- Griffin, G. and Gauthier, C. (2004). Incorporation of the principles of the Three Rs in wildlife research. *ATLA* 32 (Suppl. 1), 215-219.
- Home Office (2000). *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986*. London, HM Stationary Office.
- Krajowa Komisja Etyczna (2000). Skala Inwazyjności Badań na Żywych Kręgowcach. Komitet Badań Naukowych (www.kbn.gov.pl).
- LASA (2004). *Guidance notes on retrospective review: a discussion document prepared by the LASA Ethics and Training Group*. M. Jennings and B. Howard (eds.) Laboratory Animal Science Association.
- Mech, L.D. and Barber S. M. 2002. A critique of wildlife radio-tracking and its use in national parks. A report to the U.S. National Park Service.
- Mellor, D. J., Reid, C. S.W. (1994) Concepts of animal well-being and predicting the impact of procedures on experimental animals. In *Improving the Well-being of Animals in the Research Environment*. Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZC-CART), Glen Osmond, South Australia.
- Orlans, B. F. 1990. Animal pain scales and public policy. *ATLA* 18, 41-50.
- Orlans, B. F. 1993. *In the Name of Science / Issues in Responsible Experimentation*. Oxford University Press.
- Orlans, B. F. 1996. Invasiveness scales for animal pain and distress. *Lab Animal* 25, 23-25.
- Orlans, B. F. 2000a. Practical applications of animal harm scales: international perspectives. In M. Balls, A-M. van Zeller and M. E. Halder (eds.), *Progress in the Reduction, Refinement and Replacement of Animal Experimentation*. Elsevier Science.
- Orlans, B. F. 2000b. Public policies on assessing and reporting degrees of animal harm: international perspectives. In M. Balls, A-M. van Zeller and M. E. Halder (eds.), *Progress in the Reduction, Refinement and Replacement of Animal Experimentation*. Elsevier Science.
- Porter, D. G. 1992. Ethical scores for animal experiments. *Nature* 356, 101-102.
- Purves, K. E. 2000. Global harmonization of pain and distress classification systems: current analysis and opportunity for change. *Journal of Applied Animal Welfare Science* 3, 49-61.
- Smith J. A. and Boyd K. M. (eds.) 1991. *Lives in the Balance / The Ethics of Using Animals in Biomedical Research. The Report of a Working Party of the Institute of Medical Ethics*. Oxford University Press.
- USDA/APHIS 1991. Annual report of research facility. APHIS form 7023.
- USDA/APHIS 1997. Animal Care Policies (Painful Procedures – Policy # 11).

Acknowledgments

I thank Prof. Horst Spielmann (ZEBET, Berlin) for his generous invitation to the Congress and his great help in promoting 3Rs in Poland. I greatly appreciate the input from Robert Baker (Department of Primary Industries and Resources of South Australia), Derek Fry (Home Office, UK), Ulrika Hansson (Stiftelsen Forskning utan Djurförsök / The Swedish Fund for Research Without Animal Experiments), Roman Kolar (Akademie für Tierschutz, Deutscher Tierschutzbund), Su Hua Leow (Agri-Food & Veterinary Authority, Singapore), Yukihisa Matsuda (Akita University), Kai Pelkonen (Ministry of Agriculture and Forestry, Finland), and Dan Scholfield (Animal Welfare Information Center, USDA).

Correspondence to

Andrzej Elzanowski
Department of Zoology
University of Wrocław
21 Sienkiewicz Street
50335 Wrocław
Poland
e-mail: elzanowski@biol.uni.wroc.pl



Current Status of Establishing the 3Rs Concept in India

Shiranee Pereira

CIBA, Indian Council of Agricultural Research, Chennai, India

Summary

The CPCSEA (Committee for the Purpose of Control & Supervision of Experiments on Animals) is a statutory body of the Government of India and draws its powers from the Prevention of Cruelty to Animals (PCA) Act of 1960. The Act states that the “duty of the committee is to take all such measures as may be necessary to ensure that animals are not subject to unnecessary pain and suffering before, during and after the experiment” and “experiments on animals be avoided wherever it is possible to do so if other devices and the like may equally suffice”. This can be traced as the first legal indication of the concept of alternatives in India. The PCA Act of 1960 was conceptualised by Rukmini Devi Arundale, theophist and philosopher, a contemporary of the founders of the classical concept of the 3Rs – W. M. S. Russel and R. L. Burch. The “Breeding of and Experiments on Animals (Control & Supervision) Rules 1998” were notified in the gazette of India in 1998. These rules further reiterate the concept of alternatives. The CPCSEA proactively works to propagate the concept of the 3Rs and an independent expert committee has been constituted to suggest and implement alternatives in research, education and drug testing. There is a profound difference today, especially in the use of animals in education, in the use of equines in the production of immunobiologicals, in the manufacture of tissue culture vaccines, LD₅₀, etc. The CPCSEA, in 2004, has further officially accepted the concept of the 4th R – “Rehabilitation” of laboratory animals, stating that investigators have a moral responsibility to take care of laboratory animals after use.

Keywords: India, PCA Act, CPCSEA, three Rs, the 4th R

Introduction

In India, the concept of alternatives, though not rigidly referred to as the concept of the 3Rs, had its first indications in the Prevention of Cruelty to Animals (PCA) Act of 1960. Undoubtedly borne from India’s religious and cultural traditions and philosophy of “Ahimsa” or “non-violence”, the reference to the use of alternatives to animals in education and research was also a reflection of the personal beliefs and philosophy of Rukmini Devi Arundale, theophist and philosopher, the architect of the PCA Act.

Most Indians regard all forms of life as equally important, considering them incarnations of a single energy or life force. On a still higher plane, Hindu mythology endowed the gods with animal attributes. The lord Ganesh (the elephant god) is inseparable from his little mouse friend, Shiva cannot be worshipped without his garland of serpents, Krishna cannot be pictured without his cows, Goddess Saraswati, the goddess of wealth, is inseparable from her swan, and Lord Rama could not have been Rama without the Hanuman, the monkey god.

Hence, in a country where animals and spirituality are so intermeshed, it was a paradox and shock when the CPCSEA (Committee for the Purpose of Control & Supervision of Experiments on Animals), the statutory body of the government of India, under the chairpersonship of Madam Maneka Gandhi, in the year 2000, exposed the appalling conditions of animals and animal houses in laboratories across the country. Unfortunately, laboratories in independent India were referred to as “temples” and scientists as the “high priests”. But what transpired in these temples was far from god or religion. The sacredness of life and the concepts of Dharma (Mercy), Karma (as you

sow, you shall reap) and Ahimsa (non-violence) had no place here. It was a scenario in which thousands of animals were bled, bludgeoned, maimed and mutilated, starved and thirsty, caged and concussed, for no purpose or panacea, and their deaths saw no claims, patents, cures or curbs (Veeraraghavan, 2004). To quote Maneka Gandhi, Ex-Chairperson of the CPCSEA, “India needs to look at its scientists and put a stop to the present state of directionless, unmeaningful, sub-standard and cruel research. How valid is biomedical research in India? This is not a human vs. animals issue. The issues that I have raised having nothing to do with the cruelty to animals by itself. They are about the lack of science.” (Pereira, 2002)

The Evolution, history and current status of the concept of 3Rs in India

CPCSEA was founded by an act of the Indian parliament and draws its powers from the Prevention of Cruelty to Animals (PCA) Act of 1960. Section 17 (1) of the Act states that the “duty of the committee is to take all such measures as may be necessary to ensure that animals are not subject to unnecessary pain and suffering before, during and after the experiment”, which in spirit is the concept of the 3Rs of Russel and Burch (1959). The Act further indicates the replacement of animals in experimentation stating that “Experiments on animals be avoided wherever it is possible to do so if other devices and the like may equally suffice”.

For over three decades after the first CPCSEA was constituted in 1964, little was done to alleviate the suffering of laboratory



animals in India. Apparently, the committees failed to impose the laws and a dismal scenario continued in laboratories across the country (Pereira et al., 2004).

In 1998, under the committed chairpersonship of Maneka Gandhi, a pro-active secretariat of the CPCSEA was created. With the power to promulgate its own laws to ensure the humane and ethical use of animals in research and education, the CPCSEA in 1998 notified the “Breeding of and Experiments on Animals (Control & Supervision) Rules 1998”, which were further amended in February 2001.

From 1999, CPCSEA enforced the laws and for the first time in the history of independent India there is now a profound difference, especially in the use of animals in education, in the use of equines in the production of immunobiologicals, in the manufacture of tissue culture vaccines, LD₅₀, etc. The CPCSEA, in 2004, further officially accepted the concept of the 4th R – “Rehabilitation” of laboratory animals, stating that investigators have a moral responsibility to take care of laboratory animals after use.

Education

In recent years there has been an awakening and a realisation in academia of the profound negative impact and futility of using animals in education from both a pedagogic and a psychological point of view. It has been recognised that fear, anxiety and revulsion are imposed on the psyche of a young mind by compulsory vivisection. The questions posed were: “Is education legitimising harm and death? To a young mind, is the biology class the first lesson of violence? Can the beauty of life and living things be taught through death? Is it not a paradox of education?”

An issue bordering on human rights and a child’s right or desire not to kill or harm, however, needs more compulsive thought and urgent attention by further education boards in India.

In August 2000, the Indian School Certificate (ISC) Board for Education, one of the largest national bodies for secondary education in India, decided, “Dissection of animals will not be a component of biology practicals from the year 2000”.

In April 2001, the Central Board of Secondary Education (CBSE), India’s largest national body for primary and secondary education decided to “delete all experiments relating to dissection of animals in biology practicals in the senior school curriculum” in all CBSE schools across India.

In 2003, the Pharmacy Council of India, the academic body that governs the 300 odd pharmacy colleges in India, issued a directive to adopt the use of the “Expharm CD”, which is a full and direct replacement to the use of animals in the teaching of pharmacology, on the request of the CPCSEA.

In August-September 2004, a training course on the use of alternatives in education was organised in 11 cities in India. Over 800 academia across India, veterinary medicine, pharmacology, life sciences and medical universities, were invited to send their representatives to a training workshop and seminar entitled “Alternatives, Animal Welfare and the Curriculum”. Over 400 teachers were trained in the use of about 22

alternatives, which can directly replace the use of animals in veterinary medicine, pharmacology, medical and life science education.

In 2005, as a result of its long-term liaison with the CPCSEA, the Department of Life Sciences of Bharathidasan University, one of the premier universities in India, introduced a 95% ban on the use of animals in life science teaching.

Research

With the establishment of an active secretariat of the CPCSEA, the “Breeding of and Experiments on Animals (Control & Supervision) Rules 1998” was imposed on every establishment and breeder using or breeding animals for the purpose of education or research. The Concept of the 3Rs was introduced as the inevitable scientific solution to credible research. In the year 2000, the CPCSEA put together a national subcommittee for the promotion and propagation of the concept of alternatives in education, basic biomedical research and regulatory testing. This resulted in over 900 laboratories registering with CPCSEA. Ethics committees have been constituted in all registered institutes, honorary CPCSEA nominees have been appointed in these institutes, a special expert committee at the national level has been appointed to scrutinise and approve the use of large animals, a national “Good Laboratory Practice” document was introduced, a mandatory protocol for the care and use of equines in the production of immunobiologicals has been imposed, and the credo of 3Rs was introduced as part of every project proposal and as a legal requirement. Validated alternatives (ECVAM and ICCVAM) have been recommended to regulatory authorities, the Ministry of Health has been urged to place a national ban on the Semple vaccine, and hundreds of laboratory animals have been rehabilitated.

In March 2004, a representation from the scientific community to the CPCSEA requested that existing national norms on laboratory animal care and use be amended, so as to exclude rats, mice, birds and farm animals from all/any kind of regulation. Apropos this, the CPCSEA constituted a Consultative Group, comprising representatives from the Ministry of Health, Ministry of Science and Technology, National Research Councils, premier research institutes, philosophers and animal welfare personnel to consider this issue. The consultative group elucidated, first, the principles that should form the framework in order to review the existing norms and for the promulgation of new norms.

To facilitate the discussions, an order of relative sentience of the different species was first formulated. It was agreed on consensus that any being higher than a cockroach, representing the invertebrate, would require regulation. Thus mice, rats, birds and farm animals will *not* be excluded from regulation (Pereira et al., 2005). A further five new principles in elaboration of the 3Rs were formulated for the reduction of the use of animals, refinement by way of mandatory use of analgesics and anaesthetics, guiding principles if animals have to be euthanised and the mandatory need to rehabilitate laboratory animals after use.



The establishment of the concept of the 4th R – rehabilitation of laboratory animals

The concept of the 4th R - rehabilitation of laboratory animals was borne in India out of the urgent need to provide relief and succour to ailing animals in laboratories. Rehabilitation is undertaken when the need arises with the sole intention of alleviating any form of suffering or pain and/or to save the life of the animal (Pereira and Tettamanti, 2005). In 2004, the CPCSEA incorporated the concept of the 4th R into its official guidelines, stating that:

“Personnel using experimental animals have a moral responsibility for the animals after their use. Investigators are responsible for the aftercare and/or rehabilitation of animals post-experimentation, and may be permitted to euthanise animals only in the following situations:

- When the animal is paralysed and is not able to perform its natural functions, it becomes incapable of independent locomotion and/or can no longer perceive the environment in an intelligible manner.
- During the course of the experimental procedure, the animal has been left with a severe recurring pain, wherein the animal exhibits obvious signs of long-term extreme pain and distress.
- In situations where non-termination of the animal experimented upon would be life threatening to human beings or other animals.

Investigators are responsible for animals even after termination of the experiment and they have a moral obligation to ensure that experimental animals should be rehabilitated at the end of the experiment.

Costs of aftercare and/or rehabilitation of animals post-experimentation are to be part of research costs and should be scaled per animal in positive correlation with the level of sentience of the animals.” (Anon, 2004)

In 2004, I-CARE (International Centre for Alternatives in Research and Education), an NGO working to promote the cause of the 3Rs and dedicated to the 4th R, was created to give positive reinforcement and presence to the use of alternatives in research and education in India.

It was created recognising the need of the hour and the fact that compulsion cannot sustain positive change. Sustained change can only be achieved if every individual of the scien-

tific community is convinced that the use of alternatives is better and progressive, and that the humane use of animals in experimentation is innate to credible research. Teachers should realise that the use of alternatives in education is pedagogically superior, environmentally friendly and preserves the sensitivity of the student. The rationale behind the establishment of this centre is to empower individuals to make this change and to take positive initiative in making humane and responsible choices.

References

- Anon (2004). Report of the Consultative Group on Review of the Norms and Practices for Regulation of Animal Experimentation. Ministry of Environment and Forests, Animal Welfare Division, Government of India.
- Russel, W. M. S. and Burch, R. L. (1959). *The Principles of Humane Experimental Technique*. London: Methuen.
- Pereira, Shiranee (2002). Labs or Torture hovels. *Manushi* 132, 12-16.
- Pereira, Shiranee, Veeraraghavan, Sonya Ghosh, Sonya and Gandhi, Maneka (2004). Animal Experimentation and Ethics In India: The CPCSEA Makes a Difference. *ATLA* 32, Supplement 1, 411-415.
- Pereira, Shiranee and Tettamanti, Massimo (2005). Ahimsa and Alternatives – the concept of the 4th R. The CPCSEA in India. *ALTEX*, 22 (1), 3-6.
- Pereira, Shiranee, Tettamanti, Massimo and Bodnariu. Alina (2005). “Sentience – The basis for new laboratory animal welfare policies in India.” Poster presented at the International Conference “From Darwin to Dawkins: the science and implications of animal sentience”. London, March 2005. Organized by The CIWF, UK.
- Veeraraghavan, Prema (2004). Ahimsa Annihilated. *AAVS Magazine*, Fall 2004, 14-15.

Correspondence to

Shiranee Pereira
Consultant, CPCSEA, Animal Welfare Division
Ministry of Environment and Forests, Govt. of India
CIBA, Indian Council of Agricultural Research
75 Santhome Hg. Road
Chennai 600 028, India
e-mail: shiraneep@hotmail.com



The 3Rs in Brazil

Ekaterina A. B. Rivera

Biotério Central-Universidade Federal de Goiás, Goiânia, Brazil

Summary

In Brazil scientists, teachers, students and technicians have a new approach when working with animals due to the principle of the 3Rs. It is possible to clearly notice the changes in their attitudes towards animals, showing respect and treating them as sensitive beings and not as objects as they used to do some years ago.

Keywords: Brazil, three Rs

Introduction

Brazil is a young and continental country and for this latter reason you can find different economical, social, cultural and educational statuses. This principle also applies to the scientific field, where you have areas of excellence in some regions and in others very little knowledge of the same subjects. In relation to the 3Rs we had been working restlessly trying to reach the whole country. It is not an easy task because there are many different ways of thinking among users of animals.

Methods

A strategic plan, trying to spread the principle of the 3Rs, has been developed and it involves 4 different main areas:

1. Universities and Research Institutes
 2. Brazilian Regulatory Agencies
 3. Financial Agencies
 4. Scientific Magazines and Journals/Congresses
1. Universities and Research Institutes – The first step was to try to achieve our goals through education and there is no better field to sow than at Teaching Institutions. The importance of the 3Rs in research, education and tests has been emphasised through lectures, workshops and seminars. Courses for post graduation students as well as for technicians are given in many Institutions. Various alternatives to the use of animals in teaching and research have been introduced in our Universities and Research Centers. The creation of Ethical Committees in almost every University has helped to improve the implementation of the 3Rs.
 2. Toxicity testings in animals for the assessment of new chemicals are mandatory before their introduction in the country and are required by the Ministry of Health and the Ministry of Environment. These tests follow OECD and EPA guidelines.
 3. The Brazilian Research Council and other Financial Agencies do not approve projects which involve animals if these pro-

jects are not submitted to an Ethical Committee. The same applies to some of our Scientific Magazines and Journals.

Conclusions

There has been a great change among users of animals and the culture of care is now a common practice in the great majority of our Universities and Colleges. This is due mainly to the implementation of Ethical Committees in almost every institution where animals are used. A sharp decrease in the number of animals used in teaching programs has been noticed and an increase of more than 75% in the use of alternatives instead of animals in practical classes. The students are aware that alternatives are the future and they prefer them instead of using animals, saying that they feel more comfortable not using animals in their classes.

The Brazilian Regulatory Agencies have a modern and very good legislation regulating the required tests to assess the risk of new chemicals. From time to time these regulations have been reviewed and there is a tendency to eliminate some of the tests in order to reduce the number of animals used. When the law was first issued in 1990, 12 tests were required; in 1994 and in 1996 some of the tests were only conditionally required or bibliography could be accepted (tab. 1). Our Regulatory Agencies are very interested in applying the 3Rs. They require the contract testing laboratories to work in a GLP system and to have well trained technicians. The purpose is to use less animals, looking for alternatives to traditional tests without compromising animal and human health.

Financial Agencies, mainly the Brazilian Research Council, and scientific magazines and journals have an important role in the improvement of the 3Rs. They require that scientists submit their papers to Ethical Committees before giving their projects or papers. Ethical Committees require the 3Rs to be observed otherwise the paper will not be published or the project will not get financial support.

In 1992 we promoted an International Congress of the Brazilian Laboratory Animal Association, and the main theme of

**Tab. 1: Required tests with animals/Ministry of Health-Ministry of Environment**

Test	14/03/1990	21/12/1994	15/101996
AcuteOral toxiciy	X	X	X
Acute Dermal	X	X	X
Acute inhalation	X	X	CR
Acute dermal irr	X	X	CR
Acute eye irrit	X	X	CR
Repeated 28 days in rodents			X
90 days oral rodents	X	X	CR
90 days oral dogs	X	X	CR/B
Chronic Toxicity*	B	B	
Metabolism			X
Sub-chronic inhalation	X		
Sub-chronic dermal	X	X	

*Decretos do IBAMA- 1990, 1994, 1996, Brazil

the scientific program was the 3Rs. During the Congress we also gave a prize for the best paper on alternatives in education and another one to alternatives in research.

Other seminars, congresses and workshops have the 3Rs as their main subject or at least they are part of the program.

Implementing the 3Rs has been continuous and hard work, but it has been worth doing it. The results are more and more encouraging keeping us stimulated to continue this work. Every day more and more people get in touch with us who are interested in the subject and asking how they can apply the 3Rs. We can say, with no doubt, that Brazil is a country which, in a near future, will be using less animals in research, testing and teaching, refining the procedures used and looking for alternatives to the use of animals whenever possible.

Thus, as mentioned before, Brazil will speak the same scientific language as other countries.

This is a descriptive work, based on data of some inquiries made by the Brazilian Veterinary Association and some personal observations and reports sent by people working in the area.

Correspondence to

Ekaterina A. B. Rivera

Biotério Central-Universidade Federal de Goiás
Goiânia, Brazil

e-mail: e.rivera@uol.com.br