

The national centre for the replacement, refinement, and reduction of animals in research

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Animals have contributed to humanity in many important areas including disease research, development of new medicines, and safety testing. The routine study of animals has become essential in science in order to comprehend the basics of

anatomy and physiology and for understanding the body in health and disease.

The widespread use of animals has brought to the fore the issue of possible suffering endured by animals during experiments and how this outweighs the potential benefits of animal research. In most countries, strict regulations govern the use of animals, this ensures that animals are used only when necessary and are properly handled before, during, and after experiments. This modality has also given impetus to the development and use of non-animal 'alternative' methods including the study of cells and tissues grown in the laboratory, computer-modeled systems, and human patients, volunteers or populations.

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In their book, *The Principles of Humane Experimental Technique*, first published in 1959, W.M.S. Russell and R.L. Burch proposed the concept of the 3 Rs. The 3 Rs stand for *Replacement, Reduction, and Refinement*. Replacement alternatives refer to methods which avoid or replace the use of animals with alternative techniques. Reduction alternatives refer to any strategy that will result in fewer animals being used and Refinement alternatives refer to the modification of experimental procedures to minimize pain and distress, and to look after the welfare of the animal. Over the past 40 years the 3Rs have become widely accepted ethical principles, and are now embodied in the conduct of animal-based studies throughout many countries in the world.

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3RS) was set up in UK in 2004 as an independent organization and is responsible for supporting animal experimentation in the UK through the application of the principles of replacement, refinement, and reduction (3Rs). The website of the organization is hosted as www.nc3rs.org.uk.

Navigation of the website is best accomplished by first accessing the Information Portal that contains links to online databases, websites, journal articles, legislation, and other publications. These resources are replete with information on how to apply the principles of the 3Rs in order to accomplish the best practices in animal welfare. The information resources on this page are grouped into topical clusters which provide fairly detailed descriptions of the major issues in animal research. The common resources include various standard databases, information on anesthesia, euthanasia, ethical issues, and legislations. The portal is an essential resource for searching for existing methodologies in animal experimentation as well as looking for alternative methods which may obviate the need for animals in a given experiment. Handling of animals, information on individual experimental animals, breeding and care, genetic manipulation and related technical issues also form a part of this page. An exhaustive list of measures for assessing humane endpoints and animal welfare can also be accessed from this page.

The Centre-led Programmes link hosts information on funding opportunities for 3Rs research and also an assortment of ideas on various aspects of animal use. Methods for replacing animals for multisystem reflex studies namely nausea and vomiting, cough and gastro esophageal diseases which hitherto have been carried out only on conscious animals is addressed. The scope of tissue engineering as a means for *in vitro* studies and a replacement for animals is also discussed in-depth. NC3RS also reviews all proposals submitted to major research organizations from academic institutes in the UK in order to weed out unethical, wanton and unjustified use of animals and suggests alternatives. This initiative is carried out

in collaboration with various charitable organizations working for animal welfare.

One of the major users of animals in research is the pharmaceutical industry. An international initiative of the organization works with scientists and working groups from Europe, the USA, and Japan to identify and develop opportunities to minimize the animal use in acute toxicity studies, regulatory toxicity studies of new drugs, discovery process of monoclonal antibodies, pharmacokinetic prediction studies and for studying the abuse potential of drugs. The applications of the 3Rs to these studies are given as examples. The issue of animal testing in the chemical and consumer industry, perceived as a major segment for potential ethical dilemmas and consumer protests, is also tackled by forming active collaborations with leading chemical and consumer industries. The focus is on developing alternatives to acute oral, dermal and inhalation toxicity, skin and eye irritation and skin sensitization, tests commonly required under regulatory schemes for chemicals and agrochemicals.

The webpage entitled Experimental Design and Statistical Analysis hosts the Animal Research Reporting *In Vivo* Experiments (ARRIVE) Guidelines. These guidelines meant for improving standards of reporting from animal experiments have been developed by the NC3RS and consists of a checklist of items which act as a guide for authors and peer reviewers. The list has been adopted by most of the leading journals including the *JPP*. Other notable inclusions are Pilot Studies and Systematic reviews of animal research which tend to address the issue of “predictability and transferability of animal models” as suggested by various apex committees on animal welfare in the UK.

The Animal Technicians Support link addresses the training needs of technical staff and goes on to link two microsites—on blood sampling and another on administration of substances to laboratory animals (<http://www.procedureswithcare.org.uk/>) developed in collaboration with the Institute of Animal Technology (IAT). The issues of Rodent and Non-human Primate welfare are taken up on different webpages with a focus on guidelines, ethical issues, and refining the care of these commonly used animals.

Asister website <http://www.crackit.org.uk/> is a new initiative aimed at solving problems related to animal research by the simple strategy of posing a challenge, cracking a challenge, and finding a solution. This site forms an interface between academic scientists and the industry and helps uncover new opportunities in collaboration and for funding.

The Funding Schemes links to grants available to UK-based scientists interested in research on the 3Rs. The research portfolio of the previously funded projects makes interesting

reading and provides an insight into the quality of research done on replacement of animal experimentation.

Guidelines on ethics, toxicity studies, non-human primates and genetically altered rodents are available on the News and Publications page. The page also hosts the news in relation to activity of the NC3RS, corporate publications, journal articles, and an archive of the periodic newsletter. The most interesting link is to the Invited Articles that tackle issues related to animal experiments as viewed by eminent scientists and contains a sprinkling of write-ups on recent advances in the 3Rs. Actual examples of diseases such as multiple sclerosis, spinal cord injuries, and asthma are given with an emphasis on the adherence to the 3Rs.

This comprehensive website succeeds in providing a clear and accessible solution of most of the quandaries associated with animal research and various experimental techniques. Any researcher who wishes to embark upon animal experiments should visit the site to discover guidelines and search the linked databases to perfect the study protocol in order abide to the universal principles of replacement, refinement and reduction.

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