

THE CHALLENGE OF ANIMAL RESEARCH

Many areas of medical, veterinary and biological research depend on the use of animals. An important challenge is to develop scientifically robust non-animal alternatives, and where animals must still be used, to minimise numbers and suffering – principles known collectively as the 3Rs. The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) was established by the UK Government to address this challenge and bring benefits to science, innovation and animal welfare

NC3RS

What are the 3Rs?

The 3Rs are a framework for conducting scientific experiments humanely. The NC3Rs has adopted the following definitions:



- **Replacement** refers to methods which avoid or replace the use of animals defined as “protected” under the UK Animal (Scientific Procedures) Act 1986. These can be absolute replacements (e.g. computer modelling, *in vitro* methods, human volunteers) or relative replacements (e.g. invertebrates, such as fruit flies and nematode worms)

- **Reduction** refers to methods which minimise animal use and enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals, thereby reducing future use of animals (e.g. improved experimental design, modern imaging techniques, sharing data and resources)

- **Refinement** refers to improvements to husbandry and procedures which minimise pain, suffering, distress or lasting harm and/or improve animal welfare (e.g. environmental enrichment to improve the living conditions of research animals, anaesthesia and analgesia for pain relief, non-invasive techniques)



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Why are the 3Rs important?

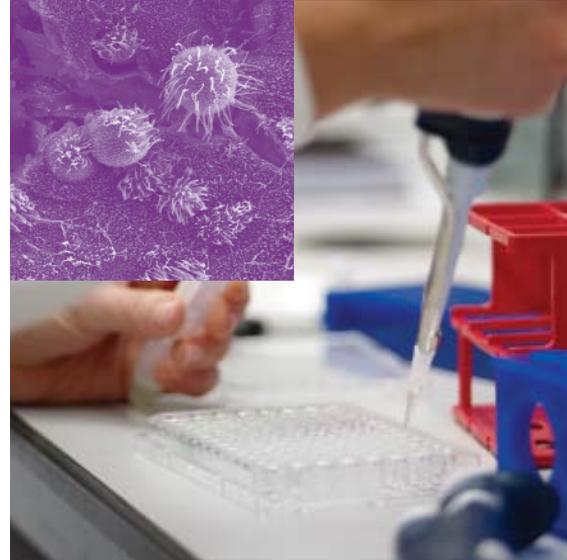
The 3Rs are important for a variety of reasons:

- **Scientific:** Applying the 3Rs can benefit science (see *3Rs in practice*)
- **Legislative:** The 3Rs are embedded in national and international legislation which protects animals used for scientific purposes
- **Ethical:** There is an ethical obligation to ensure that any harm caused to animals used in research is kept to an absolute minimum
- **Public support:** Opinion polls show that public support for animal research is conditional on applying the 3Rs

What is the NC3Rs?

The NC3Rs is an independent scientific organisation:

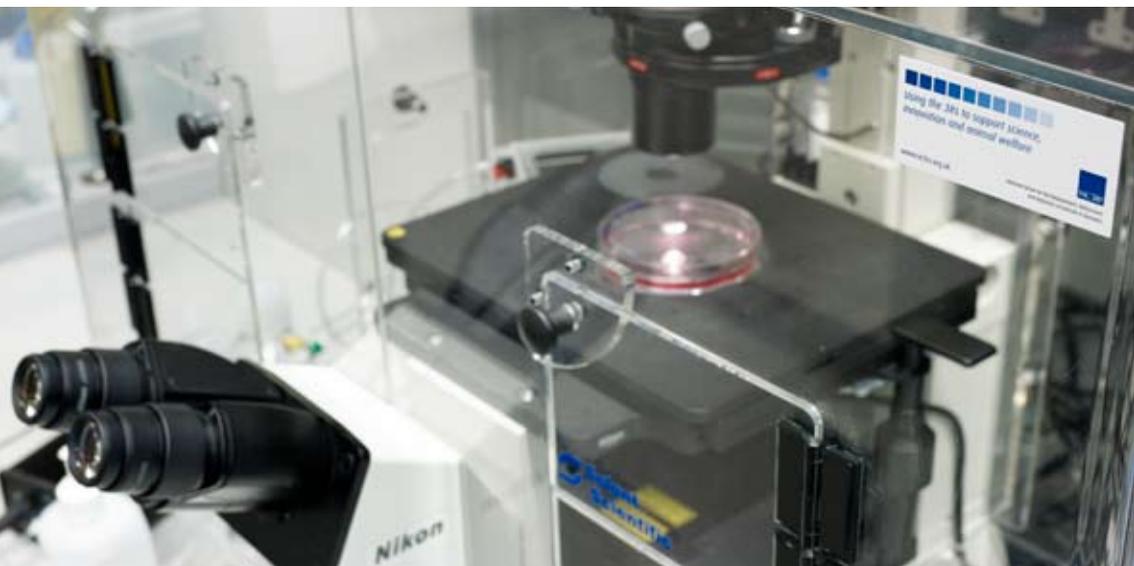
- We have an annual budget of around £4.5m
- We are the UK's largest funder of 3Rs research
- We work in partnership with bioscience research funders, academia, industry, regulators and animal welfare organisations, both in the UK and internationally, to maximise our impact
- We are funded by the organisations listed on the back cover



Inset image ©Dr Kelly Bérubé/Cardiff University

3Rs in practice: Harnessing the power of tissue engineering

The NC3Rs awarded a prize to scientists from the Lung and Particle Research Group at Cardiff University's School of Biosciences for their work developing 3-D lung tissue cultures constructed from human cells. The cultured tissue is similar in appearance and behaviour to that of the human airway, and accurately mimics natural responses to tissue damage. This 3-D tissue offers a more physiologically relevant system than animal-based methods and is being used to model respiratory injury, repair and disease mechanisms.



What does the NC3Rs do?

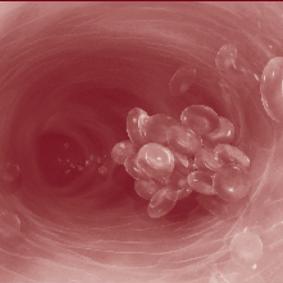
The NC3Rs has an extensive and diverse portfolio of activities which focus on areas where there is a need or an opportunity to advance the 3Rs (www.nc3rs.org.uk/programmes). These involve:

- **Driving new approaches** – by inspiring scientists and fostering innovative thinking. For example, we are leading ambitious projects to replace animals in the study of multi-system reflexes, using nausea and vomiting as a model case, and to reduce non-human primate use in developing monoclonal antibodies
- **Aligning science and technology with the 3Rs** – by bringing together experts from a range of disciplines and sectors to explore the 3Rs potential of new or under-exploited technologies and approaches. For example, using tissue engineered products to replace animals, and greater use of existing toxicokinetic data to reduce and refine animal use in the chemical industry
- **Stimulating changes in practice** – by working with scientists and regulatory authorities to review and highlight opportunities for further implementation of the 3Rs. For example, reducing the number of animals undergoing acute toxicity testing in safety assessments of pharmaceuticals and chemicals, and improving the welfare of macaques used in neurophysiological studies involving food or fluid control
- **Integrating 3Rs research into the mainstream life sciences** – by funding high-quality 3Rs research in universities and industry
- **Working with the UK's major funders of bioscience research** – to help them implement the 3Rs, through peer review and guidelines linked to terms and conditions on grants, and joint funding calls in priority research areas
- **Organising and funding events** – including scientific symposia and focused workshops as part of our integrated programmes, which provide unique forums for discussion and interaction on the 3Rs (www.nc3rs.org.uk/events)
- **Recognising and rewarding excellence** – for example, by awarding an annual prize for a publication that has positive 3Rs and scientific impacts (www.nc3rs.org.uk/3Rsprize)
- **Profile-raising and information dissemination** – via our comprehensive website, range of publications, peer-reviewed journal articles and expert working groups

3Rs in practice: Using imaging to minimise animal suffering

With NC3Rs funding, scientists at Imperial College London have developed a refined mouse model of pulmonary embolism that also reduces the number of animals needed. Using imaging techniques, the team can study the disease and evaluate treatments

by following the development of blood clots and embolisms in anaesthetised mice in real time. Previously, it was necessary to induce painful and fatal pulmonary embolisms in conscious mice. Additionally, the data generated with the new model is more representative of the early stages of the disease which makes it valuable in the search for treatments.



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Funding opportunities

Currently we have three routes for investing in research:

■ 3Rs Research Funding Scheme:

For hypothesis driven and applied research projects of up to three years that will advance knowledge and application of the 3Rs (www.nc3rs.org.uk/researchfunding)

■ Small Awards Scheme:

Provides funds of up to £3k to support small-scale projects, exchange visits and training in the 3Rs (www.nc3rs.org.uk/smallawards)

■ PhD Studentship Scheme:

Aimed at encouraging early career researchers to embed the 3Rs in their research, and to disseminate these benefits as they progress through their research careers (www.nc3rs.org.uk/studentships)

For more information on these schemes, including remit, closing dates and previously funded projects, see www.nc3rs.org.uk/fundingschemes



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Website

Access to contemporary, relevant and high-quality information underpins effective implementation of the 3Rs. In addition to information on our funding schemes and activities, the NC3Rs website features a number of unique resources:

- **Information Portal:** Contains a wealth of scientific and technical information for applying the 3Rs in research and testing with animals (www.nc3rs.org.uk/informationportal)
- **Events Calendar:** Highlights national and international 3Rs-related events (www.nc3rs.org.uk/eventscalendar)
- **Invited Articles:** To raise awareness and stimulate discussion of topical issues, new technologies, and research which advances the 3Rs (www.nc3rs.org.uk/articles)
- **Blood Sampling Microsite:** Contains information to assist with choosing the most appropriate technique for humane blood sampling from research animals (www.nc3rs.org.uk/bloodsamplingmicrosite)



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3Rs in practice: Sharing data to avoid redundant tests

In an NC3Rs collaboration with 18 European pharmaceutical companies and contract research organisations, data-sharing revealed that the number of mice or rats used per study in the single dose acute toxicity test could be substantially reduced. This resulted in a 70% reduction in animal use for this test among the companies involved (equating to approximately 15,000 fewer animals per year). Further analysis found that the test, which has used lethality as an end point in the safety assessment of new pharmaceuticals, is redundant because the information required could be obtained from other less harmful tests conducted as part of the drug discovery process. This finding has informed the revision of the international regulatory guidance for acute toxicity tests.



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To keep informed about our activities, and receive the latest news on funding deadlines, events and publications, subscribe to the NC3Rs e-newsletter at:

www.nc3rs.org.uk/signup-newsletters.asp

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