



National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

Our Strategy 2017-2019



Foreword

It is now 13 years since the NC3Rs was launched to provide scientific leadership to accelerate efforts to replace, reduce and refine the use of animals in research ([the 3Rs](#)). The unique approach that we have taken has led to a major shift in how the 3Rs are perceived across the scientific community and an unprecedented level of activity that has influenced research practice, policy and regulations, nationally and internationally. The 3Rs are no longer an aspiration, or confined to the ethical debate about animal use. Rather, we have demonstrated that the 3Rs provide a real opportunity for supporting high quality science that leads to benefits for animals, humans, the environment and the economy.

We have made significant progress in positioning the 3Rs at the heart of mainstream science. There is, however, much more to be done to realise the full potential of the 3Rs. Many areas of science are dependent on the use of animals and while technologies are emerging that have 3Rs benefits, most are a long way from routine use. Changing practice and regulations, even where there is evidence to suggest 3Rs approaches are better, can be a frustratingly slow process. Animal research is not always conducted to the highest standards, and there are still significant knowledge gaps about how to improve animal welfare.

We have previously published [our vision](#) for the 3Rs for the period 2015 to 2025. This sets out our goals focusing on five inter-related themes:

- **Practice** in the biosciences: current and future trends affecting animal use
- **Procedures** on animals: understanding the impact of research on animal welfare and its relevance to scientific quality
- **People** in the biosciences: supporting individuals to accelerate change
- **Places** conducting animal research: embedding the 3Rs in the organisational culture
- **Policy** related to animal research: influencing the global environment

Here, we summarise the NC3Rs strategy for delivery of the five 'Ps' over the next three years, 2017 to 2019. The strategy builds on our successes to date of funding high quality 3Rs R&D, establishing new partnerships with research funders, regulatory bodies and industry, investing in early career researchers, fostering multi-disciplinary and team science approaches to the 3Rs, addressing major issues affecting the reproducibility of animal studies, providing comprehensive advice and information resources, and championing cross-company and cross-sector data sharing.

In the strategy, we primarily focus on expediting the route to "mature" 3Rs impacts¹. In our experience delivering mature 3Rs impacts is a lengthy and complex process with multiple stakeholders to influence. There are many factors which affect success even when the 3Rs model or approach is published and fit-for-purpose. These factors operate at the level of the individual and, for example, include reluctance to shift from the established "gold standard" because of concerns about alienating reviewers; at the laboratory level because of the availability of skills, funding and equipment; at the institutional level because active engagement in the 3Rs is rarely recognised in career progression; and at national and international levels because of differing regulatory requirements and perceptions of the importance of animal welfare.

The NC3Rs was established by the Government in 2004 to accelerate the development and uptake of technologies and approaches which minimise the use and suffering of laboratory animals (commonly referred to as the 3Rs). It is the UK's major funder of 3Rs research, fosters industry/academic collaborations to commercialise 3Rs technologies and drives changes in policy, practice and regulations relating to animal research. It has an annual budget of around £10 million with the majority of its funding coming from the MRC and BBSRC, with additional support from Government departments, research charities and the pharmaceutical, chemical, agrochemical and consumer product industries.

Further information can be found on our website: www.nc3rs.org.uk

¹ As defined in the [NC3Rs evaluation report](#).

Practice in the biosciences

The NC3Rs vision is that research trends in the UK do not lead to an increase in animal use or suffering. This is an ambitious goal given the current and emerging drivers for animal research, such as the availability of genome editing tools. Tackling priorities for improving human health, from dementia to infectious diseases, will also demand more animal research. Nevertheless, concerns about the design, analysis and reporting of animal studies and their translation to humans have been highlighted in recent years. The so-called “reproducibility crisis” is a major issue that has implications for animal use.

We have championed an exciting pipeline of technologies with 3Rs potential. A significant challenge, however, is the wide gap between the development of new 3Rs technologies and approaches and their adoption into routine use – a 3Rs equivalent to the “valley of death” that is observed in the translation and commercialisation of basic science. The barriers to uptake are often complex and relate to a lack of awareness of, or confidence in, 3Rs approaches.

We will strengthen our links with other research funders

Decisions made by the research funders influence the scale and nature of animal research. We already work closely with many of the public and charitable funding organisations, but our strategy is dependent on strengthening these links.

- We will convene a new funders’ group comprising the major research funders to provide an annual forum for identifying the most effective 3Rs strategy in specific priority areas and a platform for seeking co-funding opportunities with the NC3Rs that better allow us to build critical mass in specific areas. This will complement our existing peer review service that we provide for the major research funders. We will seek to expand the list of funders to whom we provide 3Rs advice.

We will continue to fund the best 3Rs science

Research funding will continue to be a major incentive for academic scientists to engage in the 3Rs as well as providing the scientific and technological innovations required for progress. Supporting multi-disciplinary approaches and engaging disciplines not normally involved with animal research (such as mathematics and material sciences) have been key to our success to date.

- We will maintain the total number of grants we award over the next three years at around 30 per annum across all of our response-mode schemes. This will be dependent on the number and quality of applications we receive and our ability to secure additional co-funding.
- We will build capacity and capability by introducing an annual highlight notice to target areas where we wish to receive applications, with those reaching our high quality threshold receiving a “strategic uplift” at the funding panels. Rather than having a highlight notice aligned with a particular funding scheme as we have done in the past, we will instead have a highlighted theme running for a set period (typically a year) which will apply across all of our schemes.
- We will appoint a new impact group comprised of senior representatives to advise on strategies and approaches to further maximise the 3Rs impacts arising from our funded research.

We will boost the commercialisation of 3Rs technologies

Since 2011, our open innovation programme [CRACK IT](#) has delivered new opportunities for collaboration between industry and the SME and academic sectors, generating new knowledge, products, services and improved business processes with 3Rs and economic impacts. CRACK IT includes a challenge-led R&D funding competition ([CRACK IT Challenges](#)) and a technology partnering hub ([CRACK IT Solutions](#)).

- We will expand CRACK IT to accelerate the development of 3Rs technologies past the proof-of-concept stage so that they are fit-for-purpose in a variety of contexts and environments and available as off-the-shelf products (or services) that are easy to access.
- We will launch the CRACK IT innovation platform, a new website for showcasing the latest technologies with 3Rs potential to end-users and investors, driving their technology-readiness through collaborations, seed funding and challenge-led R&D.
- We will maintain our total funding commitment to support new CRACK IT Challenges at £2.6 million per annum, and increase the seed funding budget for CRACK IT Solutions to £0.25 million per annum. The latter will allow awards to increase from £30k to £50k for each technology showcased through CRACK IT Solutions.
- We will introduce a new business development scheme for additional funding of up to £50k for organisations funded through CRACK IT Challenges to allow them to maximise their business strategy for near-market ready products and services, such that they have (i) further validation of their technology to increase customer confidence for market entry, (ii) a portfolio of clients and prospective clients, and/or (iii) a product scaled to a level appropriate for attracting investment capital.
- We will publish a review of the 3Rs, scientific and commercial impacts of CRACK IT to date.

We will build confidence in 3Rs methods

The adoption of 3Rs technologies and approaches can be problematic. Scientists can be reluctant to change practice. Mechanisms which de-risk the transfer of knowledge, skills and expertise and allow scientists to develop confidence and experience are essential.

- We will introduce a skills and knowledge transfer scheme to cover exchange visits to other laboratories, equipment and consumable costs to facilitate the transfer of new 3Rs methods and technologies between laboratories and institutions, and workshops and other resources which address wider training requirements. Four awards of up to £75k will be available per annum.
- We will continue to work with Stevenage Bioscience Catalyst and other partners nationally and internationally to expand opportunities for the development and application of standards in 3Rs technologies and approaches. This will include improved dosing strategies for *in vitro* models, experimental design and best practice in *in vitro* model development and reporting, and providing access to reference compounds for the benchmarking of new technologies.

We will work to improve the reproducibility of animal research

We are at the forefront of efforts to tackle issues related to the rigour and reproducibility of animal research, with our [ARRIVE reporting guidelines](#) and online [Experimental Design Assistant](#) (EDA) which provides tailored advice on experimental plans. There is, however, still much to do and in our experience many researchers remain unaware of the scale and impact of the problem, or that their methods of design and analysis may be flawed.

The ARRIVE reporting guidelines are now endorsed by more than 1,000 journals. Endorsement takes a number of forms from active enforcement at the peer review stage through to simply referring authors to the guidelines. This means that compliance is patchy and the time and resources it takes for journals to check adherence to the ARRIVE guidelines are often cited as barriers to full uptake.

- We will commission the development of a tool, based on the ARRIVE guidelines, that will be freely available for journals (and authors) to screen manuscripts to assess their reporting quality. The tool will also be appropriate for use retrospectively by funders and institutions to check the quality of their researchers' publications.
- We will review the ARRIVE guidelines checklist, based on current levels of compliance and feedback from the scientific community, to ensure that the guidance provided remains appropriate for the needs of researchers.
- We will continue to increase the use of the EDA, including through the addition of new functionality, as well as raising awareness of how the system can be used. To support this, we will develop e-learning resources on experimental design aligned to the EDA.
- We will work with research funders and journals to ensure that the EDA 'diagrams' and critique provided by the system can be submitted with grant applications and manuscripts as evidence of robust consideration of experimental design and analysis.

We will facilitate the publishing of 3Rs impacts

There is little quality information published on 3Rs advances in the scientific literature. This is true of much of the work arising from NC3Rs-funded research where publications tend to describe new findings using the novel approach or technology rather than the approach itself. This is a missed opportunity for sharing information on how to apply the 3Rs and hampers wider uptake since there is rarely a realistic evaluation of the 3Rs potential.

- We will work with F1000Research to provide a platform for NC3Rs-funded researchers to publish their method development in order to provide enough detail to enable other research groups to adopt it. This will ensure that all of the work supported by the NC3Rs, including negative and null findings, is published and in the public domain.





Procedures on animals

The NC3Rs vision is that objective measures of animal welfare are routinely used to benefit the lifetime experience of animals and to improve scientific quality. Promoting animal welfare is a fundamental part of the NC3Rs remit. We have provided an evidence base and tools to support improvements to laboratory animal welfare across a range of research fields and scientific procedures. There is a need to ensure that these are used in practice. In our experience, there is still a lack of awareness among many involved about the latest refinement opportunities and how to put them into practice, and in some cases a reluctance to question and challenge established practices and cultures. As a result, standards can vary even within institutions, and there is often a long lag time between development and uptake.

We will help to ensure refinements are put into practice

There are a wide range of opportunities for refinements including improvements to housing or husbandry, the choice of outcome measures and humane endpoints, and modifications to surgical techniques and other procedures. There are similarly a wide range of stakeholders. These can have different needs in terms of information requirements and priorities. For example, often for veterinarians and animal care staff the primary consideration is how does "refinement X improve animal welfare?" while for scientists the focus is "will it introduce a new research variable or have a cost implication?". Over the years, many refinements have been based on anecdote or experience and there is a real need to support the adoption of best practice with an evidence base.

- We will continue to fund high quality refinement research. We will target areas where there are significant knowledge gaps, such as identifying early and subtle indicators of poor animal welfare, and continuing to exploit technological opportunities that can be used to improve and automate the monitoring of animal welfare.
- We will publish a review of the outputs and impacts of our refinement research.
- We will continue to focus on issues which affect animal welfare as well as scientific outcomes, such as rodent handling techniques, and widely used species such as mice, rats and zebrafish, in addition to species about which there is special concern, such as non-human primates.
- We will engage laboratory animal professionals by strengthening our collaborations with organisations such as the Institute for Animal Technology and the Laboratory Animal Science Association, in order to ensure that the materials we produce are widely disseminated, visible to those working in animal facilities and translated into practice.
- We will implement novel ways of engaging the animal technician community, for example, by using data crowdsourcing to better understand and address common problems that affect animal welfare such as aggression in male mice, and providing creative solutions to areas that have traditionally received little attention such as rat housing.
- We will organise an annual meeting of UK toxicologists working under the Animals (Scientific Procedures) Act 1986 to share best practice between companies and contract research organisations and to raise awareness of relevant NC3Rs refinement activities.
- We will take a "back to basics" approach building on the information resources we already have put in place. This includes expanding the online refinement resources we provide, such as [Procedures with Care](#) and adding others which also include a training and assessment element, for example, building on the e-learning resources that we have funded on anaesthesia and the assessment of pain, suffering and distress.

People in the biosciences

The NC3Rs vision is that all scientists understand the benefits of the 3Rs to their own research and are committed to advancing the 3Rs. Many scientists recognise that engaging in the 3Rs adds value to their work that goes beyond the ethical and regulatory considerations with which they are normally associated.

Efforts to advance the 3Rs, however, are not always aligned with drivers for scientific career progression and this can stifle participation and innovation because there is insufficient recognition of personal contributions. Progress in the 3Rs often requires sustained commitment, whereas the priorities of most scientists, regardless of their career stage, are more immediate and focused on the next grant or publication. Consequently, it can be perceived as 'safer' to stick with the model or approach that their laboratory or their field has always used, not least because of concerns about comparison with previously generated data, and there can be little incentive to engage in new or improved 3Rs approaches.

We will enhance our support for early career researchers

Support for early career researchers through our PhD studentship and fellowship schemes is critical to ensuring that the 3Rs are embedded in the scientific process, including in the training and development of future principal investigators and decision makers (from peer reviewers to heads of research).

- We will increase to 20 the number of PhD studentships we are able to award each year. We will only be able to achieve this through new funding partnerships such as that we have established with the British Heart Foundation.
- We will introduce a new training fellowship scheme for promising early career researchers with less than three years' post-doctoral experience. The scheme will focus on gaining new skills and a breadth of research experience relevant to the 3Rs. We aim to award up to six training fellowships each year.
- We will update our existing David Sainsbury Fellowship scheme. This will include changing the eligibility criteria and allowing candidates to apply for a salary commensurate with their experience as well as up to £30k per annum for directly incurred research costs. We aim to award up to three David Sainsbury fellowships each year.

We will enhance training opportunities in the 3Rs

In the UK, many scientists' first exposure to the 3Rs is through the training courses for project and personal licence holders. There is an opportunity to ensure that all scientists are better engaged from the outset and understand the scientific value and relevance of the 3Rs to their research.

- We will work with trainers and accreditors to provide dedicated material on the 3Rs, including the launch of an online tutorial on the 3Rs to be used in licensee training courses.
- We will improve training opportunities in the 3Rs across the board which will involve working with the research funders and learned societies on opportunities for continuing professional development. This will include widening access to the NC3Rs Summer School for PhD students outside of our funded cohort.
- We will partner with world-leading research groups to enable training on specific techniques or models which have 3Rs potential, including through our new skills and knowledge transfer funding scheme.

We will improve recognition of personal endeavours in the 3Rs

There is a general shift emerging in attitudes to the metrics that are used to evaluate scientists' performance. The "publish or perish" culture is starting to be challenged with some research funders recognising that quality and rigour are as, if not more, important than novelty and publications in high impact factor journals. Developing a non-animal model, or carefully designing and running an experiment with age appropriate animals takes time and the benefits may not be immediate. Focusing on the 3Rs is not always rewarded in the current system and the wider cultural shift is essential for increased scientific engagement.

- We will convene an expert group to advise the NC3Rs and the scientific community more broadly on what steps could be taken to better enhance the link between engagement in the 3Rs, personal and professional development and career progression.

Places conducting animal research

The NC3Rs vision is that all universities and other research institutions have a framework for supporting the 3Rs that delivers benefits to scientists and animals. The extent to which the 3Rs are implemented within UK research institutions varies, despite funding body expectations, the regulatory framework and external accreditation. There are a number of reasons for this including the size, culture and complexity of some organisations. In many institutions, the focus on 3Rs can be fragmented and most do not systematically collate or benchmark their 3Rs activities.

We will support institutions to actively promote the 3Rs

Many organisations are recognising the need to do more on the 3Rs, not least to protect their reputations, and we have seen an increase in the number of requests for help and advice from research institutions particularly within the academic sector. The issue of incorporating the 3Rs (or aspects such as experimental design) in the Research Excellence Framework has been raised by a number of organisations.

- We will appoint five regional NC3Rs programme managers to help institutions to implement a culture that actively promotes the 3Rs and engages staff at all levels of responsibility. The regional staff will have a number of roles including: providing expert advice on the 3Rs, raising awareness and disseminating the work of the NC3Rs, organising workshops and other events targeted to local needs, and encouraging 3Rs research and knowledge exchange at a regional level.
- We will develop a free online institutional 3Rs self-assessment tool which will allow organisations to benchmark and track their 3Rs activities and progress. The tool will focus on the following themes: leadership, people, research and infrastructure, experimental design and reporting, training, and publications and wider dissemination. It will include tailored feedback and examples of good practice. We will also develop a complementary tool for research groups to use, based on the same principles.

Policy related to animal research

The NC3Rs vision is that scientists, research organisations and regulatory bodies based in different countries work together to advance the 3Rs. The lack of global harmonisation of regulatory requirements is a major hurdle to the 3Rs and a barrier for pharmaceutical, chemical, agrochemical and consumer products industries that operate in multiple markets.

A number of large initiatives including the US Tox21 and OECD Adverse Outcomes Pathway programmes are exploring the use of mechanistic-based approaches for risk assessment. However, there remains a significant gap in establishing how these new approaches and different types of information (for example, genomic, proteomic and metabolomic data as well as improved consideration of exposure) can form part of an integrated approach to predict toxicity risk for decision-making purposes.

Validation of new test methods remains a long and complex process, which often focuses on assessing individual methods in isolation and benchmarking against historic animal studies. The process needs to be modernised to accommodate the new approaches and novel data sets being developed.

We will take on the challenge of global harmonisation in regulatory testing

Although the NC3Rs was established a national activity, we have a strong track record of collaborating with organisations based outside of the UK, including from elsewhere in Europe, the USA and Asia. We have well-established programmes with the pharmaceutical, chemical, agrochemical and consumer products industries focusing on embedding the 3Rs in R&D pipelines, which have led to changes in international regulations as well as internal company practice. Many organisations globally, including regulatory bodies, are engaged in activities with direct or indirect relevance to the 3Rs. There is the potential for a duplication and overlap and it is important that the work of the NC3Rs continues to be collaborative and add genuine value.

- We will appoint an international “ambassador” for our 3Rs in toxicological and safety science programmes to ensure that we maintain and build on our connections with other relevant activities, particularly those in the USA.
- We will work with international partners to define the global challenges for harmonisation and develop a roadmap for change that focuses on identifying redundant tests and optimising the use of non-animal approaches. This will include a new initiative with the European Commission's Joint Research Centre and the US National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) on accelerating the global elimination of the acute toxicity “six-pack”, as well as building on our ongoing partnership with ILSI Health and Environmental Sciences Institute on mathematical modelling in toxicology and exposure science.
- We will apply our experience in the development of evidence-based recommendations to areas such as juvenile toxicity studies for pharmaceuticals, acute toxicity for chemical formulations and reviewing the added value of using two species for toxicity testing.



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