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

Our Vision 2015-2025

Pioneering Better Science

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Introduction

The NC3Rs mission is to replace, refine and reduce the use of animals in research.

We work in partnership with the research community to drive changes in animal use and deliver measurable impacts in the 3Rs. Our aim is to improve scientific outcomes, stimulate regulatory change, address societal concerns about animal welfare and provide new opportunities for commercialising 3Rs technologies. We focus on areas where animal use or suffering is high, where there are significant questions about the utility of the *in vivo* models, or where emerging technologies present an opportunity to advance the 3Rs.

Our approach to date has been from the top down, to shape and respond to the scientific, regulatory and political landscape and from the bottom up, to empower scientists at an individual and organisational level to change practice. Our view is that the most significant gains in the 3Rs will come from voluntary engagement informed by scientific and evidence-based arguments. To support this we have funded research and training, championed an open innovation approach to the development and commercialisation of 3Rs technologies, and facilitated data sharing and knowledge exchange for evidence-based changes in policy, practice and regulations.

Here we set out the NC3Rs vision for the next ten years focusing on five inter-related areas: Practice, Procedures, People, Places and Policy. This holistic approach is essential to move the 3Rs agenda to the next level.

The NC3Rs vision

Practice in the biosciences: current and future trends affecting animal use	Vision for 2025: Research trends and investment in the UK do not lead to an increase in animal use or suffering
Procedures on animals: understanding the impact of research on animal welfare and its relevance to scientific quality	Vision for 2025: Standardised objective measures of animal welfare are used routinely to benefit the lifetime experience of animals and to improve scientific quality
People in the biosciences: supporting individuals to accelerate change	Vision for 2025: All scientists understand the benefits of the 3Rs to their own research and are committed to advancing the 3Rs
Places where animal research is carried out: embedding the 3Rs in the organisational culture	Vision for 2025: All universities and other institutions have a framework for supporting the 3Rs that delivers benefits to scientists and animals
Policy related to animal research: influencing the global environment	Vision for 2025: Scientists, research organisations and regulatory bodies based in different countries are working together to advance the 3Rs

Delivering the NC3Rs vision will require our science programmes to be expanded and will depend on collaboration with a range of individuals, organisations and sectors. In this document we primarily focus on working with scientists. We use the term scientist to refer to those in academia and industry who lead programmes of work involving the use of animals or whose expertise could be relevant to advancing the 3Rs, including mathematicians, engineers and chemists. We also recognise that our continuing engagement with funders, regulators, animal care staff and veterinarians is essential.

The NC3Rs vision has been developed based on our experience to date, horizon scanning and literature reviews, and interviews with key opinion leaders from across the scientific community. We are grateful for the advice and guidance provided by all of those who have helped shape our future work.

A summary of the information collated to support the vision is presented in Tables 1 and 2.

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Practice in the biosciences: current and future trends affecting animal use

Vision for 2025: Research trends and investment in the UK do not lead to an increase in animal use or suffering

We will:

- Respond to changes in the bioscience sector that will impact on future animal use
- Develop and integrate 3Rs technologies and approaches into academic and industrial research processes

1. In order to achieve the NC3Rs vision, we need to anticipate, understand and respond to changes in the scientific landscape so that we can focus on areas that are both relevant to scientists, and have greatest impact on animal numbers and welfare.

2. Over the last ten years, there has been an increase in the number of scientific procedures using animals in the UK. The main drivers of this trend have been the prioritisation of specific research areas, new regulatory requirements, the availability of new technologies such as tools to genetically modify mice and fish, and the continued reliance on animal models in many disciplines.

3. There is currently an exciting research and development pipeline of technologies with 3Rs potential. The NC3Rs has been a prominent stimulus for the creation and exploitation of this pipeline in the UK. We have identified and invested in the most promising areas for (i) replacement, including multi-disciplinary approaches which combine biology (e.g. stem cell technologies), engineering (e.g. microfluidics) and mathematics, (ii) reduction, including imaging technologies and techniques such as microsampling, and (iii) refinement, including the development of systems to better monitor animal behaviour.

4. We have also demonstrated the importance of sharing existing data sets for identifying 3Rs opportunities particularly in pharmaceutical development, and we are extending our role as an 'honest broker' for data sharing more widely into the academic sector to maximise the benefits that can be achieved.

We will respond to changes in the bioscience sector that will impact on future animal use

5. Over the next ten years the demand for animal research is likely to remain high. We predict that the research areas that will have the most impact on animal use will be infectious diseases and antimicrobial resistance, chronic illness and diseases of ageing (e.g. pain, Alzheimer's disease), oncology, genetics and genomics, new types of medicines (e.g. nanomedicines, electroceuticals) and vaccines. These will potentially drive up animal use and lead to the development of new animal models. We will continue to provide leadership in the generation of a research environment where consideration of the 3Rs is firmly embedded in decision making and day-to-day practice. We will work to ensure that the impact of research investment on animal numbers and welfare is reduced by targeting our activities and resources to provide alternative models, tools and approaches. In some areas, such as ageing, we are already working with the relevant communities and it will be important to consolidate these activities. In others, we will need to establish new collaborations or expand existing partnerships to prioritise new areas of joint interest, for example, specific fields of research or technology development.

6. In the public sector, there is increased emphasis on quality, reproducibility and measuring the impact of investment in science. These factors provide the scientific community with an opportunity to further explore the efficient use of animals and to ensure that all studies that are carried out provide value by adding to the knowledge base. Evidence suggests that many studies using animals are poorly designed, analysed and reported. We are already working closely with the research community, including funders and journals, however there is much more to do to address these fundamental issues. We will continue to facilitate an environment in which (i) both the utility of specific animal models and how they are used are frequently reviewed, so that the right model and the right study design is always used, and (ii) researchers are easily able to access and build on findings.

7. In the private sector there is a significant shift in the business model to one where much research, particularly toxicology, is outsourced. Many companies are looking to contract research organisations for innovation and therefore may reduce their direct engagement in the 3Rs. The paradigm for contract research organisations is also changing with the large, established companies increasing their investment in non-animal technologies, and new, smaller organisations providing specialist niche technology platforms. We will continue to work closely with our partners in the pharmaceutical, chemical and consumer products industries, as well as contract research organisations, in the UK, elsewhere in Europe, Asia and the US, to predict future scientific and business trends that may impact on animal use and to develop collaborative 3Rs programmes which respond to this. We will complement this with increased engagement with regulatory bodies so that the route for accepting new 3Rs methods is accelerated.

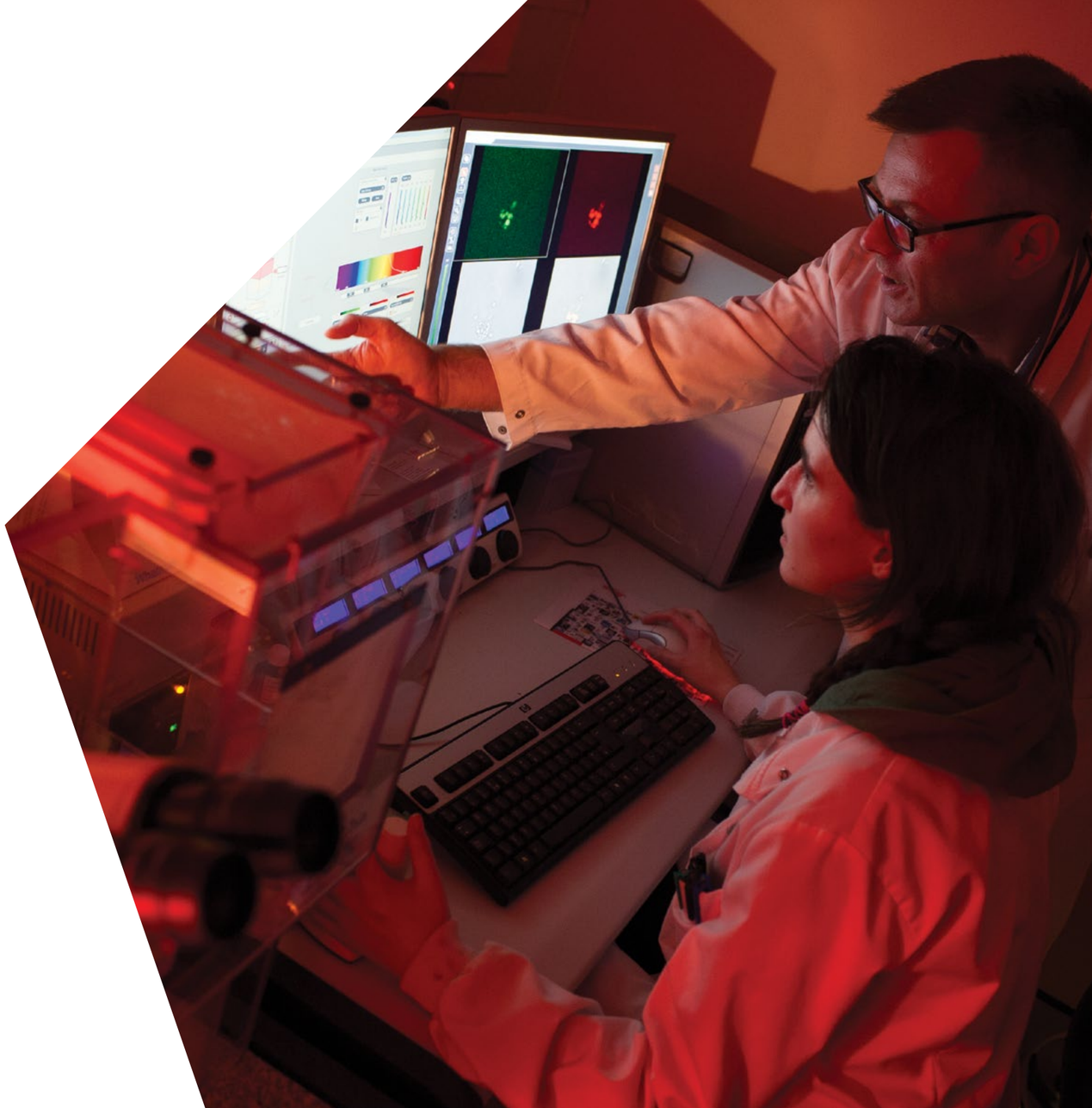
8. While in the long term we expect *in vivo* studies to be reduced in some areas, animal research will continue to be an important part of the biosciences. For some of the emerging

technologies there will be new concerns for animal welfare. We will remain vigilant of such instances so that the 3Rs benefits can be maximised and the harm to animals minimised.

We will develop and integrate 3Rs technologies and approaches into academic and industrial research processes

9. If the NC3Rs vision is to be realised, scientists need to be equipped with the necessary tools to address their research questions without animals, or using fewer animals, and with less impact on animal welfare. Over the next ten years we will continue to invest in research and other activities which give scientists more choice and more confidence in technologies and other approaches which replace, reduce or refine the use of animals.

10. There is a wide gap between the development of new 3Rs technologies and approaches, and their routine and widespread use in the academic and industrial research settings. One of the major reasons for this is that many scientists are reluctant to change practice because of how it may be viewed by their peers or regulators. The challenges are five-fold: (i) raising awareness about existing 3Rs technologies and approaches, (ii) developing new technologies and approaches past the proof-of-concept stage so that they are fit-for-purpose in a variety of environments and contexts, including for company and regulatory decision making, (iii) ensuring that new tools are not seen simply as an adjunct to *in vivo* studies, (iv) providing 'off-the shelf' products which ease access and use and (v) addressing concerns about the cost of establishing and using new technologies. We will focus on encouraging and providing new routes for the scientific community to take greater responsibility in sharing and publishing information on advances in the 3Rs; providing new mechanisms which allow scientists to transfer established 3Rs methods and technologies into their own laboratories or institutions; and expanding CRACK IT, our unique 3Rs open innovation and commercialisation platform.



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Procedures on animals: understanding the impact of research on animal welfare and its relevance to scientific quality

Vision for 2025: Standardised objective measures of animal welfare are used routinely to benefit the lifetime experience of animals and to improve scientific quality

We will:

- Reduce the impact of common procedures on animal welfare
- Support scientists to develop relevant and practical measures of welfare

11. The knowledge base on animal behaviour, cognition and emotion has expanded significantly over the last ten years, providing new opportunities to understand animal welfare and reduce suffering. We have supported this through funding research in evidence-based refinements for identifying and controlling pain for example, and by developing resources to provide practical guidance for scientists, veterinarians and animal care staff.

12. There is a moral imperative to improve the lifetime experience of animals used for scientific purposes. While many scientists recognise the importance of good welfare, this is by no means universal. There are a number of factors which limit progress in fully adopting the latest refinements including inertia, lack of awareness or evidence to support change and concerns about resource and compromising data quality.

13. There is increasing evidence to demonstrate that factors that influence animal welfare such as housing, handling and pain can also impact research outcomes. Better understanding of the links between animal welfare and scientific quality is required, and the development of better tools and more subtle measures of animal suffering is key to this. Greater evidence of the impact of welfare on data quality could provide an incentive for more widespread refinement.

We will reduce the impact of common procedures on animal welfare

14. We already facilitate the sharing of information on refinement through workshops, networking events, online resources and publications. This includes the outputs of the research we fund and our office-led programmes, as well as the information provided by others. We will take a 'back to basics' approach focusing more on the barriers to adoption and ensuring that existing information on refinement is provided in a targeted manner to researchers, veterinarians, animal care staff, regulators and ethical review bodies, including through training. We will prioritise specific areas to consolidate and embed best practice, including better use of analgesia, humane methods of euthanasia for rodents and evidence-based enrichment for fish and amphibians.

We will support scientists to develop relevant and practical measures of welfare

15. Animal welfare science is in its infancy and we will need to build capacity to deliver the NC3Rs vision and to investigate the links between welfare and quality of scientific data. There is a need for well validated methods to recognise animal suffering, clear evidence that refined approaches actually benefit animals and do not compromise scientific objectives, and practical measures of welfare that are specific to the experiment, disease model and species. We will support the development of reliable and efficient tools for assessing pain and distress and the integration of these into the laboratory setting. Our focus will be on identifying early, objective and subtle indicators of poor animal welfare, and new ways of assessing cumulative suffering.

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People in the biosciences: supporting individuals to accelerate change

Vision for 2025: All scientists understand the benefits of the 3Rs to their own research and are committed to advancing the 3Rs

We will:

- Increase the number of scientists engaged in the 3Rs
- Provide relevant 3Rs training to scientists at all stages of their career
- Expand cross-discipline and cross-sector collaborations which advance the 3Rs

16. The establishment of the NC3Rs in 2004 provided many scientists in the UK with an opportunity to actively engage in the 3Rs for the first time. Since then scientific ownership of the 3Rs agenda has gained significant momentum and demand for our resources, including from outside of the UK, has increased year on year.

17. Historically, in many areas the use of animals has been the 'default' position because alternatives have not been available. This has led to the use of animals becoming ingrained into standard practice such that it may be difficult to get funding or to publish in the absence of *in vivo* data. In our experience there are still many scientists who fail to see the relevance of the 3Rs to their research or how they can contribute to developments in the 3Rs, and who remain unaware of the latest 3Rs advances. Addressing this will be key to delivering the NC3Rs vision. We will need to build on our track record of taking a science-led approach to the 3Rs and the complex and sensitive issues related to animal research so that all scientists (i) are equipped to question the added value of *in vivo* models and their relative importance; (ii) are able to identify the research needs for the development and use of alternative *in vivo, in vitro* or *in silico* models that reduce the impact on animals and (iii) can access the resource to fulfill these needs and change their practice.

We will increase the number of scientists engaged in the 3Rs

18. The NC3Rs vision is for all scientists to have the expertise and resource to innovate in the 3Rs. We recognise this is an ambitious plan and in reality this will be an incremental process building on the foundations we have established. Over the next ten years we aim to provide all scientists in the UK with an opportunity to engage in the 3Rs by supporting primary 3Rs research and technology development, providing training opportunities through studentships and fellowships, increasing the range and visibility of information resources available to support evidence-based adoption of the 3Rs, and stimulating cross-discipline and cross-sector collaborations.

19. We will work in the priority areas we have identified to have the largest impact on animal use and welfare, and engage leaders in each of these communities to customise a 3Rs programme specific to their needs. We will continue to invest in high quality research and development to accelerate the availability of new 3Rs models, tools and approaches. Our aim is to increase the number of awards we are able to make and to maximise our investment by ensuring that all of the scientists we fund take an active role in promoting the 3Rs within their institutions and disciplines.

20. In the academic sector, we recognise it can be difficult to identify and engage relevant communities because of the diversity of the research, the small number of groups that may be working in any one area or using a specific model, and the wide laboratory to laboratory variation in practice which can make it difficult to propose standard approaches to advance the 3Rs. We will increase our local and regional presence to ensure that all academic scientists are aware of the 3Rs, the work of the NC3Rs and how their expertise can contribute to advancing the 3Rs.

We will provide relevant 3Rs training to scientists at all stages of their career

21. Most scientists are exposed to the 3Rs for the first time when applying for a project or personal licence to use animals. While the regulatory driver is important it can encourage a 'tick box' approach. We will work with trainers and accreditors to provide dedicated material on the 3Rs in order to ensure that all scientists are better engaged from the outset. One-off training, however, is insufficient and it is important to maintain up-to-date knowledge. We will continue to provide a wide range of resources for scientists to maintain expertise and interest. We will have a specific focus on fostering innovative thinking around framing scientific questions with the 3Rs embedded, as well as choosing the most relevant model and designing the best experiment. We will work with a range of organisations including research funders and learned societies and with those with relevant roles under the Animals (Scientific Procedures) Act 1986 (amended 2012) (ASPA) to ensure that resources are targeted appropriately and address the needs of specific communities. We will continue to invest in online resources such as *Procedures with Care* and the *Experimental Design Assistant* as part of our 'back to basics' approach.

22. Since 2009 we have funded 51 PhD studentships and nine early career fellowships. This small cohort is important because it embeds the 3Rs in the ethos and practice of individuals from the start of their career and we expect them to lead by example as 3Rs ambassadors within their peer groups. We plan to continue this investment in training and development and our aim is to increase the total number of awards we make over the next ten years. We will also use the experience we have gained in providing dedicated 3Rs training for our students and fellows to benefit other early career researchers. We will work with the Research Councils and learned societies to consider how best to do this, primarily focusing on those with an *in vivo* component to their training programme.

We will expand cross-discipline and cross-sector collaborations which advance the 3Rs

23. We have championed a cross-discipline and cross-sector approach to advancing the 3Rs which has brought together individuals who would not normally collaborate. In many instances this has involved scientists from disciplines outside of the biosciences, including mathematicians, engineers and chemists, who are not familiar with the 3Rs but who nevertheless have expertise that could be relevant. We provide a range of support for scientists to find the right partners to stimulate ideas, leverage new funding opportunities and combine expertise to facilitate change. This includes one-to-one partnering via our technology partnering hub CRACK IT Solutions through to cross-company data sharing initiatives involving over 30 organisations.

24. Significant potential exists to expand our model of collaboration into new areas such as transgenic technologies, systems modelling, engineering and software development. We will continue to evolve and invest in CRACK IT to stimulate new collaborations across disciplines and between industry, SMEs and academia. Supporting academics and SMEs to recognise that their research may have 3Rs potential will be critical and will build on our partnership with Innovate UK (formerly known as the Technology Strategy Board) and industry end-users to ensure that technologies emerging in the research base are 'validated' (e.g. fit-for-purpose in an industrial context) and commercialised.

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Places where animal research is carried out: embedding the 3Rs in the organisational culture

Vision for 2025: All universities and other institutions have a framework for supporting the 3Rs that delivers benefits to scientists and animals

We will:

- Support institutions to implement a culture that actively promotes the 3Rs and engages staff at all levels of responsibility

25. Over the last ten years our primary focus has been on increasing the engagement of individuals in the 3Rs and collaborating with the organisations that fund, regulate or represent them. Fostering greater engagement at an institutional level is critical to the NC3Rs vision for the next ten years and to provide a supportive environment for 3Rs activities to grow.

26. All establishments using animals in the UK are regulated under the ASPA. This sets out specific terms and conditions under which animals can be used and defines various statutory roles which have relevance to the 3Rs. While the ASPA should ensure that the 3Rs are put into practice it does not necessarily encourage scientists to actively participate in expanding the 3Rs knowledge base.

27. Many organisations are committed to exceeding the legal minima and for supporting a 'culture of care'. In our experience, however, this is not universal and there is more that can be done to support an active institutional 3Rs community which involves senior management, scientists, veterinarians and animal care staff working as teams. The recent commitment to openness endorsed by many organisations, following a drop in public support for animal research, provides a new incentive to do this, particularly in terms of managing reputational risks.

28. There are a number of barriers to greater engagement in the 3Rs at an institutional level. These include (i) concerns about escalating costs and the resource already required to meet regulatory requirements, (ii) the size and complexity of some organisations, (iii) a failure to appreciate the scientific and economic benefits the 3Rs can bring, and (iv) a view that complying with the ASPA is sufficient in terms of 3Rs activity.

We will support institutions to implement a culture that actively promotes the 3Rs and engages staff at all levels of responsibility

29. We will focus on helping institutions maximise their commitment to high quality animal research. To support this we have recently published a seven point institutional framework for the 3Rs which includes steps to recognise, promote and reward 3Rs developments. We will work with universities and other institutions to adopt and implement the framework and to share experiences on embedding it in policy and practice. We will complement this by increasing our presence at a local and regional level to (i) provide expert advice and disseminate the work of the NC3Rs, (ii) support named persons under the ASPA with the latest information on the 3Rs, (iii) horizon scan for research and technologies with 3Rs potential and connect them with potential end-users, and (iv) facilitate improved knowledge exchange across institutions.

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Policy related to animal research: influencing the global environment

Vision for 2025: Scientists, research organisations and regulatory bodies based in different countries are working together to advance the 3Rs

We will:

- Increase international scientific support for the 3Rs
- Improve global harmonisation of regulatory 3Rs practice for pharmaceuticals, chemicals and consumer products

30. Although established to accelerate national progress in the 3Rs, many of the NC3Rs programmes involve collaboration with scientists and organisations based outside of the UK. The value of international collaboration is clearly illustrated by our work with the pharmaceutical and biotechnology sectors. Working with companies and regulators from the UK, elsewhere in Europe, the USA and Asia, we have identified opportunities to reduce and refine animal use across the drug development pipeline, which have changed company practice and led to regulatory change.

31. The lack of global harmonisation of regulatory guidelines is, however, a major issue for the pharmaceutical, chemical and consumer products sectors which wish to operate in multiple markets. Changes in UK and European regulations which take account of the 3Rs do not always influence company practice as animal studies may still be conducted to meet regulatory requirements elsewhere in the world. There is considerable interest in moving to human-based systems for risk assessment with the USA leading the way in this area (e.g. through the US Environmental Protection Agency ToxCast programme and Tox21). These initiatives will provide industry with some viable non-animal approaches within the next ten years, however ensuring their global acceptance and uptake will require early engagement and collaboration with organisations such as the Organisation for Economic Cooperation and Development.

32. The NC3Rs is well recognised internationally as a resource for the 3Rs. Around 60% of the visitors to our website are from overseas. We have supported international uptake of guidelines and online resources by translation into different languages. The *Procedures with Care* website for refining commonly used procedures has been translated into Chinese and the ARRIVE reporting guidelines are available in Chinese, Portuguese and Italian and have been distributed to scientists in 25 countries.

33. Science is a global endeavour and international issues can influence policy and practice in the UK. We recognise that there is more to do internationally to improve support for the 3Rs. This is important for two reasons, first to ensure a level playing field for UK researchers and second, to support our work to commercialise 3Rs technologies and create a market for 3Rs products and services. This is a challenging goal because of cultural differences and resource requirements. Taking a collaborative, science-led and evidence-based approach has underpinned our success nationally and this will form the basis of our approach to increase international engagement and delivery of our vision.

We will increase international scientific support for the 3Rs

34. We will expand the number of scientific organisations that we collaborate with to extend our international outreach and increase the pool of scientists actively engaged in 3Rs activities. This will include creating opportunities for co-funding of research collaborations involving scientists from the UK and other countries. We will initially focus on increasing the visibility of our online resources and promoting adoption of our guidelines by funders, professional bodies and institutions, with emphasis on the ARRIVE guidelines. Promoting the scientific benefits that the 3Rs can provide will be key to our success and we will work to encourage international journals to place greater emphasis on publishing 3Rs outcomes.

We will improve global harmonisation of regulatory 3Rs practice for pharmaceuticals, chemicals and consumer products

35. We will strengthen our existing interactions with companies and regulatory bodies, and seek new partnerships with those in other countries with whom we have had little previous interaction (e.g. China, Brazil and India). We will prioritise those areas in which we have already established a programme of work, for example, on ecotoxicology, biosimilars, and intelligent dose setting for chemical toxicity and will use the emerging evidence base from these to open discussions in new geographical areas.

36. We will work with international regulators to identify new areas to collaborate on, which may include topics such as exploring the added value of a second species for chronic toxicology studies, juvenile toxicology studies for pharmaceuticals and acute toxicity for formulations of chemicals, as well as accelerating the development and acceptance of non-animal tests.

Table 1: Research priorities and trends and their potential impact on animal use*

Research priorities and trends	Potential impact on animal use
Ageing and diseases of an older population	Increase in (i) research conducted in ageing animals to translate disease and efficacy findings to humans and (ii) use of disease models in specific areas. For example, in Alzheimer's disease there is a heavy reliance on genetically modified animals (e.g. amyloid ß, tau).
Chronic diseases e.g. cardiovascular, diabetes, pain, respiratory	More *in vivo* studies for target identification and use of multiple disease models to demonstrate efficacy of new drugs. Additional welfare implications for animal models of chronic diseases.
Genetics and genomics	Continued increase in the development and use of genetically modified animals in gene function studies.
Infectious diseases	Identification of novel and high risk pathogens in humans and animals and research into their transmission and host-response could lead to increased use of new and existing animal models of infectious diseases, some of which may be associated with severe suffering.
Neuroscience	More advanced models available for basic research (e.g. using light to control and monitor neurons) and to model neurological disorders which may be used in addition to current models.
New types of medicines and products	Increased demand for animal models to test efficacy and safety of novel materials (e.g. regenerative medicine (tissue engineered or stem cell products for bone regeneration or wound healing), electroceuticals, nanotechnology, biologically-based agrochemicals).
Oncology	Predicted increase of the use of patient-derived xenograft models. Potential for stratification of human mutations and personalised medicine to increase animal use.
Safety and toxicology	Lack of focus on (i) exposure-based risk assessment and (ii) global harmonisation of regulatory guidelines could result in increased animal use (e.g. regulatory bodies in China, Russia, India and Brazil requiring more studies than EU and US). Increase in antibody-based therapies with implications for the use of non-human primates.
Vaccines	Increasing numbers of animals used to test new human and veterinary vaccines (e.g. challenge studies) and also to batch test existing vaccines during manufacturing.

Table 2: New technologies and their potential impact on animal use**

Research priorities and trends	Potential impact on animal use
Adverse Outcome Pathways (AOPs)	Use of a mechanistically-based, AOP approach to link a molecular initiating event with an adverse effect could reduce the number of animals needed for chemical risk assessment (e.g. skin-sensitisation, oxidative stress, lung fibrosis).
Automated *in vivo* monitoring devices (e.g. telemetry, video)	Intelligent cages for automated and home cage monitoring (e.g. to assess animals in their own environment). The increased use of monitoring devices will enable refinement of studies (e.g. earlier detection of toxicity or disease progression). Devices to get more information from animal studies that are already being carried out will lead to fewer animals being used in individual studies (e.g. combining safety and toxicology studies).
Bioprinting	Advanced technology has the potential to improve stem cell and tissue-based systems due to co-printing of cells and scaffolds, allowing penetration of the whole tissue construct. Liver systems to detect toxicity show the most potential to reduce animal use. The technology could potentially be used to reduce *in vivo* efficacy models (e.g. oncology).
Genetic modification e.g. CRISPR	New genome editing technologies could increase the use of species other than the mouse for genetic alteration (e.g. non-human primate, rat). Such technologies have advantages over current methods in that they use fewer animals to generate those of scientific interest.
Imaging technologies: *in vivo*	Advances will enable longitudinal measurements in the progression of disease or drug testing in the same animal, therefore reducing animal use. There is potential for larger impact if imaging technologies could be developed for use in the GLP environment (e.g. toxicology studies) and in free roaming animals (e.g. optical imaging). Miniaturisation of devices (e.g. head-mounted microscopes) could improve animal welfare. Increased use of animals in new areas (e.g. optogenetics).
Imaging technologies: *in vitro*	Advances may enable more sophisticated human relevant cell-based systems to be developed.

Table 2: New technologies and their potential impact on animal use (continued)

Research priorities and trends	Potential impact on animal use
Mathematical informatics and *in silico* modelling	Increased use of mathematical modelling in various areas (e.g. oncology, infectious diseases) could reduce animal use. Development of population-based models to extrapolate from studies in the laboratory to the real life situation in the field (e.g. ecotoxicology) will improve their validity and uptake. Use of big data and large scale bioinformatics approaches to inform *in silico* modelling approaches will increase their predictive accuracy.
Microsampling	Increased use of more sensitive methods of quantification of drugs and chemicals (e.g. mass spectrometry) enables smaller blood samples to be taken from animals. Microsampling will lead to fewer animals being used per study and has the potential to have impact across efficacy, pharmacology and toxicology studies.
Non-mammalian models	Increased use of *Drosophila*, zebrafish and cell lines from non-mammalian species (e.g. fish). Reduction in the use of mammalian species for disease modelling, safety and toxicology (e.g. reproductive toxicology). Fish metabolism studies *in vitro* could reduce the need for fish bioaccumulation testing.
Organs-on-chips, microfluidic technology	Development and use of such technologies could replace the use of animals in specific disease modelling, safety and toxicology studies (e.g. cardiovascular, kidney).
Stem cells, tissue engineering	Technology is becoming more standardised and reproducible increasing confidence in the models. Further focus on industry needs and specific input from clinicians could lead to technologies being used to directly reduce and replace animal use in specific assays (e.g. liver and cardiovascular safety studies, iPS cell tau assays for Alzheimer's disease). Basic research is increasing in tissue engineered cartilage, blood vessels, skin and cornea which may reduce animal use in these areas.

* Notes from Table 1:
A range of publically available information sources were used including from Asthma UK, Alzheimer's Research UK, Arthritis Research UK, Biotechnology and Biological Sciences Research Council, British Heart Foundation, Cancer Research UK, Diabetes UK, Engineering and Physical Sciences Research Council, Horizon 20:20, Innovative Medicines Initiative, GlaxoSmithKline, Medical Research Council and the Wellcome Trust. Information was provided from interviews with a range of stakeholders from across the scientific community.

**Notes from Table 2:
Information was provided from interviews with a range of stakeholders from across the scientific community.

NC3Rs funders

The NC3Rs is primarily funded by the Department for Business, Innovation and Skills via the Medical Research Council and the Biotechnology and Biological Sciences Research Council. It also receives core funding from the Home Office. Funding for specific posts and programmes is provided by a range of organisations from the public, private and charitable sectors.

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