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

2022-2024

Strategy

Pioneering Better Science

Foreword

This is an exciting and important time for the science and adoption of approaches to replace, reduce and refine the use of animals in research and testing (the 3Rs). Global collaboration and recent technological developments have created scientific breakthroughs that will replace the use of animals with *in vitro* and *in silico* technologies and transform the use of animals in academia and industry. The UK is playing an important role in advancing molecular and cell biology, computational science, mathematics, and other intersecting fields with the aim of creating new methodologies and non-animal technologies. Crucially, this effort is also generating the evidence required to change long-established practices.

There are many reasons for optimism, but we must also recognise the significant barriers that impede the uptake of the 3Rs. We have focused our recent work on tackling the "3Rs valley of death" in which scientific breakthroughs lack the evidence base to become widely adopted. Even when the evidence base is strong, there remains the significant challenge of encouraging practices to change. A further barrier can be the polarisation of views across society, which can inhibit open communication and collaborations that are critical to changing perceptions and practices.

Balancing these grounds for optimism and concern, we are launching a new strategy for 2022 to 2024 that is committed to accelerating 3Rs impacts and enhancing communication. Our strategy signals an increased focus on replacement science and technologies to unlock powerful human models, increase global uptake and open commercial opportunities. We will maintain our long-term approach to achieve changes in regulations and to accelerate local adoption of best practices in refinement and reduction, recognising that animal research will continue to be important for many areas of science.

We will continue to support and empower the next generation of researchers and technical and support staff in academia, industry and regulatory bodies to develop their careers through advancing the science and adopting the 3Rs. In doing this, we reaffirm our commitment to embedding equality, diversity and inclusion in our activities. Advances in the 3Rs are dependent on partnership. We will build on our 18-year history to convene and support UK and global collaboration. Progress in the 3Rs must be accelerated in all countries and the talent and determination to achieve this goal resides across many universities, public bodies, industries and charities. We will continue to provide leadership and support to bring these diverse sectors together to achieve our goals.

Finally, on behalf of everyone at the NC3Rs I would like to thank our funders and collaborators for the long-term support and relationships that make progress possible.

Professor Kevin Shakesheff
NC3Rs Board Chairman

Introduction

1. There has been rapid change in the level of interest in the 3Rs over recent years with the NC3Rs playing a key leadership role in this. This interest extends globally with the establishment of new 3Rs centres, and across sectors with the recognition of the potential benefits that replacement technologies[1] can offer to science, human health and the protection of the environment. The availability of complex *in vitro* models such as microphysiological systems and new advances in artificial intelligence technologies are providing for the first time the opportunity to make substantive and wholesale changes to the way animals are used. These are exciting times but there is much to be done to exploit and capitalise on this momentum. Significant barriers remain despite the large investments in technology development worldwide. Barriers include poor awareness about the availability of replacement approaches and a lack of confidence in how they might be used including for regulatory purposes. These are compounded by a reluctance in the research community to change practice that is in part based on the long-term polarisation of the animal research issue, and a frequent bias in the system that favours *in vivo* models over non-animal approaches.

2. Despite the advances in replacement technologies, animal research remains important in many areas of science as exemplified by the response to the COVID-19 pandemic. That said, some animal studies continue to be poorly designed, analysed and reported despite the evidence of the impact that this has on the reliability, reproducibility and utility of findings. There is increasing commitment to openness and transparency by the biosciences sector, nevertheless, public and parliamentary concern about animal use remains high. There have been major changes in the implementation of the UK's legislation on animal research and testing, with greater emphasis being placed on local institutional controls and governance, and there are concerns from some stakeholders about the possible implications for animal welfare that this may have.

3. The 3Rs are now part of common scientific parlance. Most bioscience organisations have a public facing policy on animal research and implementing the 3Rs, although the extent to which they apply this in practice varies considerably. There is often a long lag between the development and widespread uptake of 3Rs approaches. We coined the term the "3Rs valley of death" in 2017 to describe this and tackling it is a central focus of the strategy over the next three years, recognising the impact that it has on the NC3Rs mission.

4. A variety of factors contribute to the "3Rs valley of death" including the requirement for training, equipment or infrastructure and/or concerns about comparison with data from traditional models, or acceptance by others such as funders, regulators and journals. There can be inherent delays because of the time required to change regulations, particularly on the international stage where it can be difficult to achieve consensus. Even where there is a compelling evidence base, adoption

[1] We use the term "replacement technologies" to refer to both full and partial replacements as described in the NC3Rs definitions. Where we use the term "non-animal technologies", this specifically refers to full replacement only, that is, the use of human volunteers, tissues and cells, mathematical and computer models, and established cell lines.

of 3Rs approaches can be slow as exemplified by the uptake of non-aversive mouse handling methods, simple and relatively easy refinements to implement with the potential to benefit millions of animals worldwide that have nevertheless taken a decade to become common practice.

5. Supporting the development of new 3Rs models, tools and technologies is essential to the NC3Rs mission but alone is insufficient in terms of tackling the "3Rs valley of death". Our strategy reflects this and the importance of also "winning hearts and minds" by addressing cultural barriers to the 3Rs. Part of the challenge is the competing pressures that many individuals and organisations are under and a research ecosystem in which consideration of the 3Rs can be superficial or incomplete. We need to tackle sector-wide issues that impact the NC3Rs mission, and our strategy aims to achieve this by taking a leadership role and working in collaboration with partners nationally and internationally.

6. This document summarises the NC3Rs strategy for the next three years, highlighting new areas of focus that will run in parallel with ongoing long-term projects. The strategy is based on plans that we submitted, as part of the NC3Rs funding renewal, to the MRC and BBSRC and which led to an allocation of core funding of £30.3M for 2022 to 2024[2].

How we will deliver the NC3Rs strategy

7. The delivery of the NC3Rs strategy is dependent on the following activities that are intended to ensure that the UK remains at the forefront of 3Rs activities internationally and that the NC3Rs has a balanced portfolio across the 3Rs.

    a. **Funding multidisciplinary research and innovation.** We have a first-class track record of supporting the development and use of 3Rs models, tools and technologies. We will ensure that our funding schemes remain agile and able to support the pipeline from initial concept through to the comparative, validation, feasibility and reproducibility studies intended to demonstrate that the 3Rs approaches developed are well-characterised and ready for deployment.

    Through response mode funding we will continue to support the best ideas and teams as well as investing in cutting-edge technologies through the CRACK IT Challenges innovation programme. We will facilitate partnerships between our grant holders and organisations with specialist equipment and expertise to help drive the adoption of new tools and technologies for use by industry. We will establish networks to better link our grant holders with one another in areas where we have built a critical mass, such as oncology and in technologies such as microphysiological systems. Through these networks we will also work with grant holders to showcase their outputs to interested stakeholders to enable further connections and dissemination opportunities to be developed and exploited, maximising the 3Rs impacts of our research and innovation portfolio.

[2] Core funding from the MRC and BBSRC is reviewed on a five-year cycle. The latest funding settlement is for financial years 2020/21 to 2024/25. The total core budget for this period is £49.1M.

b. **Supporting training in the 3Rs.** We have championed the 3Rs in the training of early career researchers through our PhD Studentship and Fellowship Schemes, as well as providing training materials and courses that are widely used by other researchers and animal care staff.

   Training is essential to ensure the right knowledge base and skill set to accelerate the uptake of 3Rs approaches. It is also important for achieving a more critical approach to model selection and experimental design than currently happens, and for promoting greater awareness of the opportunities that already exist to improve animal welfare. For these reasons, training in the 3Rs will continue to be an important part of the delivery of the NC3Rs strategy, including funding early career researchers.

c. **Using our in-house expertise.** We have a dedicated team with the knowledge and skills to drive advances in the 3Rs that cannot be achieved by research and innovation funding alone. We will continue to work effectively and efficiently, using our connections nationally and internationally to influence change and embed the 3Rs into policy, practice and regulations. Maintaining our collaborations with research funders, regulatory authorities, industry bodies and other 3Rs centres will be essential. We will focus on the cultural barriers to the adoption of 3Rs approaches, applying the principles of human behaviour change to all of our programmes to help address the "3Rs valley of death". Underpinning this, we will continue to ensure that our communications strategy is dynamic and that the information and materials we provide are evidence-based and appropriately targeted for the intended audience. Our website has hundreds of thousands of users each year. Its size and the types of information it provides have grown substantially in recent years. We will undertake a significant overhaul of the site to improve the user experience and access to relevant content, with the goal of increasing traffic to the site by 20% (from 300,000 visitors per year), doubling the number of page views (to 1.5M a year) and decreasing the bounce rate to key resource pages by 10% by the end of 2024.

People and partnerships

8. Supporting individuals and building partnerships will be key to the delivery of the NC3Rs strategy. We already have extensive collaborations with organisations across the sector nationally and internationally and it will be important to maintain and build on these further to help embed the work of the NC3Rs into common scientific practice and regulatory decision making. We have a track record in bringing together diverse expertise and skills to collaborate on the 3Rs and we will focus on further enabling cross-sector and interdisciplinary approaches across our portfolio of activities. We are unique in the range and nature of the collaborations that we have in place and there is an opportunity to use these more effectively, for example, to facilitate new connections for our grant holders as outlined in paragraph 7a. The rise in the number of 3Rs centres worldwide represents an important shift in the landscape and we will embrace opportunities to work with them wherever possible. More broadly, we will increase our outreach activities, providing opportunities for public engagement in the 3Rs and supporting our grant holders to champion their research within wider society.

9. Supporting an inclusive and diverse working and research environment is a priority for the NC3Rs. We learn from and value the perspectives of the diverse range of collaborators and partners we work with, which in turn strengthens our activities, stimulates innovation and informs our decision making. We will ensure that our internal processes and science programmes actively embed equality, diversity and inclusion, in line with UKRI's strategy. Our staff are our most important resource and we are committed to providing equal opportunities in empowering them to achieve their full potential. We will continue to improve our ability to attract and retain a diverse and talented team and we will provide the training and support required to enable our staff to deliver the ambitions described in this strategy.

What will we deliver?

Expanding the focus on replacement technologies

10. Accelerating the use of models, tools and technologies to replace *in vivo* studies is a key goal of the strategy. Over the next three years we will further strengthen our focus in this area, concentrating on five main themes that include increasing investment in replacement technologies, setting standards for *in vitro* studies and tackling barriers to the use of non-animal derived antibodies.

Increasing the availability of replacement technologies ready for deployment in academia and industry

11. We will increase our target commitment in replacement technologies to at least £6M annually to fund a minimum of eight new projects each year. This represents approximately 75%[3] of our commitment budget for research and innovation – our goal is to use this investment to build on our track record in this area and respond to the increasing interest in alternatives to *in vivo* research from across the biosciences sector. We will continue to fund high quality science in response mode as well as targeting specific areas through CRACK IT Challenges. The latter will include work to build virtual species for toxicity testing and increasing confidence in the use of microphysiological systems, helping to underpin major reductions in the use of animals over the next decade. Investing in these so-called new approach methodologies (NAMs)[4] will be a central part of our collaboration with industry and regulators nationally and internationally. There is already considerable activity in NAMs globally and to ensure that we target our resources where we are likely to achieve the most impact, we will establish an expert steering group to advise on priority areas that we should invest in.

[3] Over the last five years, 66% of the NC3Rs budget for research and innovation has been committed to funding replacement technologies.

[4] In recent years, the term new approach methodologies (NAMs) has been adopted by the bioscience sector specifically to describe non-animal technologies for use in assessing chemical or drug toxicity.

12. We will build on existing collaborations as well as establishing new research partnerships that expedite the use of 3Rs technologies in academic and industrial settings by testing them in real-world scenarios. Securing co-funding is essential to delivering our ambitions in this area and our goal is to attract £5M over the next three years. We will ensure that our research funding pipeline continues to support the development, characterisation, validation and uptake of replacement technologies. The latter is particularly important given the significant barriers and delays that many technologies face in becoming adopted into common practice, and we will review how we target funding to best address this critical stage. We will build additional support into CRACK IT Challenges to enable more opportunities for testing and commercialisation activities. Based on industry comparators, we already have a high success rate with the number of Challenges that lead to a product or service and our goal is to increase this further from the current 63% to 75% by the end of 2024[5].

Supporting the skills base in replacement technologies

13. We will evolve our PhD Studentship Scheme so that it only supports training in the development and application of replacement technologies. This is an important step for ensuring the UK has a scientific workforce able to respond to demands from the sector for expertise and skills in non-animal technologies. By targeting our investment in this area, we will also be able to better tailor the additional bespoke training we provide to our students, including utilising our extensive industry networks to facilitate other training and development opportunities.

14. We have budgeted for 12 PhD studentships[6] a year, with up to an additional six supported with co-funding arrangements. Partnerships with Unilever and the British Heart Foundation over the last five years have allowed us to increase the pool of talented researchers we can support and our plans are dependent on continuing to secure co-funding.

Targeting areas where the uptake of alternative approaches has been slow

15. We will establish a new programme of work to tackle the issues that inhibit widespread use of non-animal derived antibodies and affinity reagents that have been available for research purposes for some years but have so far failed to disrupt the use of animal-derived materials. Recent reports by organisations such as ECVAM[7] have highlighted this as a priority area, but the response from the UK's research community has been lukewarm.

16. Our preliminary work indicates that the barriers to change are extensive, from commercial availability through to a lack of awareness of the utility of the alternatives. We will establish an expert working group that includes antibody users, commercial suppliers and technology developers to help us to map out a strategy for the UK, including the resources required from the

[5] Note 93% of CRACK IT Challenges deliver a prototype (i.e. a working model).

[6] The budget committed is £1.08M per call. Awards can be for three or four-year studentships and therefore depending on the duration of those recommended for funding by the Panel, up to 12 can be awarded.

[7] European Centre for the Validation of Alternative Methods (ECVAM).

NC3Rs, to address the "3Rs valley of death" for non-animal derived antibodies. Aligned with this, we will review our policies as a research funder on the use of non-animal derived antibodies in the work we sponsor and seek to engage other funders in this to ensure a harmonised approach.

Setting standards for *in vitro* research

17. We will publish recommendations for reporting *in vitro* studies to improve their reliability and reproducibility. The NC3Rs mission is dependent on ensuring that *in vitro* studies are properly designed, analysed and reported. Evidence suggests that issues related to internal validity and bias are commonplace in *in vitro* studies. The consequences of this are that animals may be used unnecessarily, as *in vitro* studies often inform *in vivo* studies or use primary animal cells and tissues or animal-derived products. Importantly, if the findings from *in vitro* studies are not reliable or reproducible then this has the potential to undermine confidence in the models used and ultimately affects the likelihood they will be used to replace animals.

18. We will establish an international expert group to develop the RIVER recommendations (**R**eporting ***I**n* **V***itro* **E**xperiments **R**esponsibly). Our plan is to publish the recommendations as a preprint by the end of 2022. Learning lessons from our experience developing the ARRIVE reporting guidelines for animal studies, we will initially focus on a small number of priority items essential for improving the reliability of findings described in a manuscript. This will support incremental and achievable changes in reporting practice. We will use the RIVER recommendations as a basis for engaging with publishers and journals to encourage active adoption of the guidelines into practice and our goal is to have 300 organisations endorsing their use (e.g. in editorial checks and/or guidance to authors) by the end of 2024. We will also use the recommendations as a starting point for dialogue with funders to promote greater transparency in the description of *in vitro* experiments in grant applications so that the reliability of these experiments can be fully evaluated.

Facilitating access to information on replacement technologies

19. We will develop practical guidance to support researchers in how to effectively and easily search for replacement technologies. Researchers are typically required to justify *in vivo* studies in the context of the availability of potential replacement technologies when applying for funding or seeking permission to use animals. There is a systemic lack of awareness about the availability and suitability of replacement technologies such that opportunities can be missed by researchers, and in turn, ethics committee members, peer reviewers, journal editors and regulators. This in part reflects the research ecosystem and the challenge of building confidence in the use of new approaches such that there is a critical mass of evidence to catalyse a shift away from established animal models.

20. We will launch a new programme of work to better understand the extent to which researchers search for replacement technologies, which information platforms they use and what gaps exist, so that we can provide useful guidance, including on how best to present the findings from searches to relevant stakeholders. We will have completed this work by the end of 2023.

Improving the quality and conduct of *in vivo* research

21. Although the use of replacement technologies will become more commonplace, for the foreseeable future the use of animals will continue to be required for many areas of academic research as illustrated by the MRC's recent investment in the national mouse genetics network. Changes in international regulatory requirements are also likely to drive continued animal use, including in studies involving high levels of animal suffering. Reduction and refinement remain a critical part of the NC3Rs strategy. We already have a strong track record and internationally recognised programmes in these areas. However, there is considerably more to do to ensure that all animal studies are exemplars of best practice and we are well-placed to deliver this with our in-house expertise.

Championing the robust design of animal studies

22. We will double to 20,000 the number of registered users for our online Experimental Design Assistant (EDA). We will achieve this by adding new functionality so that the EDA can support a wider range of experimental designs than is currently possible, and by updating the "look and feel" of the system to improve the user experience. In parallel with this, we will facilitate better use of the EDA for grant applications and manuscript submissions (to evidence robust experimental design), including by providing output from the system that can easily be shared via an online link. This will replace the current PDF format that is considered by some funders and journals to be incompatible with their drive to streamline the information required from applicants and authors.

Addressing knowledge gaps in experimental design

23. We will increase the training opportunities available for researchers in experimental design. Many researchers have limited knowledge and understanding of experimental design and statistics, and the factors that influence rigorous methodology. This has an impact on the way they design and conduct experiments and also how they assess manuscripts and grant proposals in their capacity as journal editors, reviewers and funding panel members. Progress is hampered by a lack of training opportunities. To address this, we will develop e-learning modules for the main factors affecting the internal validity of studies – modules on masking (or blinding) and randomisation will be available by the end of 2023 and on sample size calculation by the end of 2024. Experimental design will be a critical part of the 3Rs training framework that is described in paragraph 34 and we will work with the UK's major funders of PhD students to ensure that all those undertaking *in vivo* studies are encouraged to complete the e-learning modules.

Promoting transparent reporting of animal experiments

24. We will fund the development of a tool to automatically check compliance with the ARRIVE Essential 10 reporting recommendations for *in vivo* research, helping researchers and journals ensure that publications include all of the information required to assess the reliability of the

findings presented. The tool will be available by the end of 2024 and will be free to use. Our goal is to have at least 50 journals employing the compliance checker as part of their editorial processes in the first year following its release.

Minimising animal use in regulatory toxicology studies

25. We will continue to work with industry to provide evidence-based recommendations to reduce animal use and improve the study designs used within regulatory studies required for the safety assessment of pharmaceuticals and pesticides. This includes recommendations for appropriate group sizes and number of dose groups, criteria for species selection, and avoiding the use of additional groups of animals added for the assessment of recovery or toxicokinetic purposes. We will continue our collaboration with the US-based Health and Environmental Sciences Institute reviewing the requirements for *in vivo* endocrine tests conducted for environmental safety assessments with the goal of decreasing requests from regulators for additional animal studies. A series of papers on these areas and related topics will be published in 2023.

Evolving our animal welfare programme

26. We have a strong track record of delivering improvements in animal welfare through funding research and innovation, establishing topic-specific working groups and conducting desk-based activities led by our own scientific staff. Our experience promoting non-aversive mouse handling methods has highlighted the challenge of achieving widespread adoption of even simple refinements and the different approaches and information/evidence requirements that are needed to garner support for change from key stakeholders. Learning from this, in 2022 we will establish a new steering group to support our animal welfare programme. The group will focus on streamlining the process from the refinement concept through to delivering change in the animal facility. It will include expertise from across the sector and will be tasked with helping to identify areas for refinement activities, the best approach to take (e.g. data sharing or commissioning research) and potential barriers to uptake, including seeking early adopters and champions to build confidence in new approaches.

Improving the use of humane endpoints

27. We have funded the development of new welfare indicators for a range of species (e.g. pain faces) and digital technologies (e.g. home cage monitoring) that allow for more detailed and objective assessments of welfare. These are not yet routinely used to inform the development and implementation of humane endpoints. Generally, humane endpoints tend to be generic and use arbitrary scoring criteria that are not ideal for assessing animal welfare. We will commission a software tool that will help researchers and animal care staff identify appropriate humane endpoints based on the body system(s) involved. Our goal is for this to be available for use by the end of 2024.

Refining chemical safety assessments

28. We will publish a strategy for applying the 3Rs in fish acute toxicity testing for ecotoxicology. This is part of our wider programme to tackle the use of acute toxicity studies which involve the death of the animals as an endpoint. There is more work to do to support the use of signs of evident toxicity (rather than death) in chemical testing. We have developed guidance on the use of this refined endpoint for acute oral toxicity studies in rats and our aim is to incorporate this into the relevant OECD test guideline[8], by the end of 2024, although we will need to keep this under review given the slow timeline for regulatory change and the need for international consensus.

29. We will collaborate with industry bodies to highlight how the appropriate use of toxicokinetic approaches can inform dose selection for regulatory studies required for chemical safety assessment. This is against a backdrop of proposed revisions to European Chemical Agency advice that focus on chemical hazard identification rather than risk assessment. The revisions are likely to lead to the testing of chemicals at unnecessarily high doses, with the associated increased potential for animal suffering. In parallel we will publish guidance in 2023 for concentration setting for endocrine studies for environmental assessments.

Creating a research, policy and regulatory environment actively supportive of the 3Rs

30. The delivery of the NC3Rs strategy is dependent on us working with and influencing the organisations that fund, conduct, licence, require or publish the findings arising from animal research and testing. Over the next three years we will focus on enhancing consideration of the 3Rs in the academic sector, championing greater recognition for endeavours in the 3Rs, and addressing areas where there is an opportunity to tackle long-standing public concerns about animal use.

Improving academic engagement in the 3Rs

31. We will publish an analysis of the UK's current review and approval processes for animal research with recommendations on how these could be adjusted to better support adoption of advances in the 3Rs. The recommendations will be based on stakeholder interviews across the sector focusing on funders, regulators, ethics committee members and those working under the Animals (Scientific Procedures) Act 1986. We will map what the various regulatory and review processes and bodies currently do to ensure implementation of the 3Rs so that we can identify any gaps, flag unnecessary duplication and more effectively promote uptake of scientific and technological advances in the 3Rs. Our aim is to publish the analysis and recommendations in 2022 and use these as a basis for strengthening our engagement with the academic community, including considering how we best utilise our regional staff.

[8] OECD Test No. 420: Acute Oral Toxicity – Fixed Dose Procedure.

32. In parallel, we will continue to promote the two 3Rs self-assessment tools that we have developed for institutions and research groups to evaluate, track and benchmark their 3Rs activities. By the end of 2024 our plan is to have doubled (to 100) the number of UK establishments using the institutional assessment tool as well as achieving a five-fold increase (to 500) in the number using the research group tool. We also have ambitions to encourage international use and our goal by the end of 2024 is to have 100 overseas establishments and 200 research groups signed up. Meeting these national and international targets will require the support of regulators and funders to help disseminate and promote the tools and ultimately to encourage (or require) use.

Publishing detailed methodologies as standard practice

33. We will improve the publishing of 3Rs methodologies so that there is sufficient detail in the public domain to allow others to critique, understand and reproduce the models, tools and technologies, thus helping to build confidence in 3Rs approaches and encourage their wider use. We have previously launched the NC3Rs gateway, in partnership with the publisher F1000Research, to provide a dedicated platform for NC3Rs grant holders to publish methodologies and validation studies. We are committed to publishing a minimum of eight papers per year from NC3Rs grant holders on the gateway. In 2023, we will review with the Gateway Advisory Board expanding the platform to open it up to other organisations that fund 3Rs research, helping to support their work and fulfil the wider mission of the NC3Rs to promote the 3Rs. More broadly, there is still little motivation and few incentives for researchers to publish methodologies because of the lack of recognition and reward for this, despite the increased focus across the sector on research integrity and the importance of transparent methodologies to this. This is a barrier to the impact of the NC3Rs and we will initiate a more formal discussion with key scientific bodies to begin the work required to embed the publication of methodologies as standard practice across disciplines.

Supporting professional development and training in the 3Rs

34. We will increase opportunities for training in the 3Rs helping to build capacity and support a scientific workforce actively committed to the 3Rs. We will ensure that all eligible NC3Rs events (online and in-person) are associated with CPD points and we will work with funders and institutions to foster expectations that researchers and animal care staff will continue with professional development in the 3Rs throughout their careers. The one-off training required to get a licence to use animals in the UK is not sufficient and addressing this is an important part of the cultural change we are seeking. We will work with organisations across the sector to develop a 3Rs training framework and will allocate funding for the development of training materials (e.g. online training resources) to support this. We will commence the development of the framework in 2023, and as part of this we will launch regional training schools for first year PhD students (regardless of the funder) whose studies involve the use of animals so that they have a firm grounding in the 3Rs from the start of their careers. Our goal is to provide 3Rs training for 200 students by the end of 2024.

35. We will ensure that NC3Rs-funded students continue to receive the additional training that we have traditionally provided and that has been so valued (e.g. the annual summer school). We will continue to include bespoke training and support for postdoctoral researchers on NC3Rs grants to help them sustain a career in science. We will complement these activities with the introduction of a new scheme for NC3Rs-funded PhD students and postdoctoral researchers to access funding for dissemination activities to promote the 3Rs models, tools and technologies that they have developed – our goal is to make 20 awards in the next three years.

Harmonising adoption of 3Rs approaches

36. We will initiate new projects to tackle areas of public and scientific concern. This includes the use of non-human primates for safety testing purposes, building on our expertise and long-standing industry collaborations in this area. The increased demand for non-human primates due to the COVID-19 pandemic and concomitant export ban from China has led to concerns in the sector about shortages for regulatory testing. We will work with industry and regulatory bodies to identify current opportunities for further minimising use as well as brainstorming areas that we and others could invest in to ultimately replace the use altogether. This work will commence in 2022. In parallel, we will use the partnerships we have in place with funders and academic and industry users to develop international standards in the care and use of non-human primates, which we will publish in 2024.

37. Global harmonisation of testing requirements for pharmaceutical and chemical safety assessment will continue to be an active part of our toxicology programme. Even where there are overarching international guidelines there can be geographical variations in practice and implementation of the 3Rs. By the end of 2023 we will have completed a review of the animal-based testing methods described in WHO manuals, guidelines and recommendations for biologics and vaccines to identify where updates can lead to a more harmonised adoption of the 3Rs in batch release and post-licensure quality control testing requirements. This is an important collaboration with the WHO, supported with funding from the Bill & Melinda Gates Foundation. As part of the project, we have been tasked with identifying the barriers that exist in different geographical regions which may hinder the adoption of 3Rs approaches by manufacturers, national regulatory authorities, and control laboratories that are responsible for the testing and release of biologics and vaccines. We will use these findings as a basis for a new programme of work focusing on training and outreach activities to encourage regulators and manufacturers to change practice, as well as supporting low and middle-income countries to access the resources and expertise necessary to adopt 3Rs approaches.

Measuring impact

38. We will review the information we collect to assess the impact of the NC3Rs as a whole, as well as specific programmes and projects, including how we present this information to ensure that we are as transparent as possible, in line with our status as a mainly publicly-funded organisation. Measuring the impact of our strategy and the use of resources is essential for assessing and demonstrating the value, effectiveness and reach of the NC3Rs work. We collate quantitative and qualitative information from a range of sources, including Researchfish[9], surveys and meetings with grant holders, and we publish this on our website or in thematic reviews with accompanying case studies. In 2010, we published an evaluation framework for the 3Rs which we have used across our activities. This has served us well, however we now plan to update it in line with the ambitions in this strategy and this will be a focus for 2022.

[9] Researchfish is an online system used to collect research outputs.

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