



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

Annual Report 2016

Pioneering Better Science

About the NC3Rs

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) is a scientific organisation that leads the discovery and application of new technologies and approaches that minimise the use of animals in research and improve animal welfare (the 3Rs).

We collaborate with scientists and organisations from across the life sciences sector, nationally and internationally, including universities, the pharmaceutical, chemical and consumer products industries, other research funders, and regulatory authorities.

We support the commitment of the scientific community to the 3Rs by funding research and early career development, facilitating open innovation and the commercialisation of 3Rs technologies, and stimulating changes in policy, regulations, and practice.

Further information can be found at www.nc3rs.org.uk

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Foreword

2016 was an exciting year for the NC3Rs. It included the appointment of two new regional programme managers to support the implementation of the 3Rs on the ground. The new posts are co-funded with higher education institutions and we are very pleased to be collaborating with the Universities of Birmingham, Leicester and Nottingham (the Midlands group) and the Universities of Liverpool, Manchester and Sheffield (the North West and Yorkshire group) on the first appointments. Our aim is to ultimately establish regional posts across the UK.

In December, we held a workshop to review the outputs of four grants we had previously awarded to explore the utility of non-mammalian models such as *Drosophila* and zebrafish larvae for asthma research. The workshop highlighted the 3Rs impacts of these models as well as the new scientific insights they can provide, for example, on mucosal inflammation following infection, and the role of asthma susceptibility genes.

The awards are part of the £8.3 million that we have committed to date to support the development and characterisation of non-mammalian models for replacing and reducing the use of other animals, primarily rodents across research areas as diverse as neuroscience, cardiovascular sciences, cancer, and toxicology, and our plan is to build on this establishing a critical mass to fully exploit their 3Rs potential.

The 2016 3Rs prize, which is generously sponsored by GlaxoSmithKline, beautifully illustrated the importance of generating an evidence base to support refinements. The winning paper from a team at the University of British Columbia in Vancouver reported research on the importance of behaviours such as rearing, stretching and burrowing for laboratory rats.

The research could have a transformative effect on future housing and husbandry practices and how we can help facilitate this will be a focus for 2017 when we launch our year of 'laboratory rodent welfare'.



Although the NC3Rs was established as a national organisation much of our work and focus is inevitably international.

In March, we participated in the third Sino-British International Seminar on Research Animal Welfare and Ethics in Hefei, China. The event, organised by the UK Government and Chinese Association for Laboratory Animal Sciences aimed to equip laboratory animal professionals with the practical tools to apply the 3Rs in their work and institutes. We were able to use the event to launch Chinese (Mandarin) versions of our grimace scale posters and the pocket-sized ARRIVE guidelines which we were able to produce with funding from the Home Office.

We have also been doing the ground work for new initiatives for 2017, including new funding schemes. These will focus on driving impact and ensuring that 3Rs technologies and approaches are used in practice. Our success is dependent on the funding we are able to secure and we would like to take this opportunity to thank the organisations from across the public, charitable and industrial sectors, and particularly the MRC and BBSRC who continue to be our major funders, for their financial support.

Dr Vicky Robinson CBE
NC3Rs Chief Executive

Professor Stephen Holgate CBE
NC3Rs Board Chairman

Funding research and early career awards

In 2016, we continued to fund projects, early career researchers and infrastructure through our various response-mode funding schemes. These schemes are a critical part of our strategy to deliver new 3Rs research models and tools to the scientific community and to build a critical mass of individuals engaged in the 3Rs in the academic sector.



In total, in 2016 we committed £5.3 million to 16 institutions across the UK.

Project grants

We funded seven project grants totalling £2.35 million. The projects included the development of a non-mammalian model for toxicity testing of inhaled nanomaterials, an *in silico* model of human dorsal root ganglion electrophysiology for use in pain research, and a tool for improved welfare assessments in fish. A list of the 2016 awards can be found in Annex 1.

Strategic awards

We made one award under our strategic call for refinements in the use of chronic implants in macaque neuroscience studies. The award of £214,565 to Professor Alex Thiele and colleagues at Newcastle University complements previous work we have funded in this area, also at Newcastle University, including the development of a non-invasive Head Immobilisation System for macaques that was published in the *Journal of Neuroscience Methods* in 2016.

PhD Studentships

Eleven awards, totalling almost £1 million, were made including one sponsored by the British Heart Foundation as part of a joint collaboration with the NC3Rs that was launched in 2015. The annual summer school for first year NC3Rs-funded PhD students was held at the University of York. Seven non-NC3Rs funded PhD students from the university also participated in the two-day event which focused on providing skills and training to ensure a solid foundation in understanding the scientific importance of the 3Rs.

David Sainsbury Fellowships

Three fellowships were awarded in 2016 taking the total number of fellows to 13. The awards were for projects to support the use of intestinal organoids as a replacement for mouse models in whipworm research, the development of 3D structures called gastruloids to study the process of left/right asymmetry during embryonic development, avoiding the use of mouse embryos, and new methods to assess visual perception in mice based on their spontaneous behaviour which should reduce the number of animals used.

Infrastructure for Impact awards

We previously introduced the Infrastructure for Impact scheme to recognise the importance of funding 3Rs infrastructure such as networks, equipment, databases and online resources. In 2016, we made three awards totalling £1 million. These included funding for the infrastructure necessary to expand the use of human tissue to replace the use of some animal studies in asthma and respiratory disease research. The award was to a team led by Professor Maria Belvisi at Imperial College London and importantly included collaborators at the UK's NHS Blood & Transplant and NHS Tissue and Eye Services,

which is responsible for coordinating, recovering, processing, banking and supplying human tissue for transplantation.

Other awards included funding to support an international network of scientists and regulators to accelerate the use of human-based *in silico* approaches for cardiotoxicity testing, and the optimisation of sperm freezing and distribution methods to avoid the transport of male *Xenopus laevis* frogs, again through an international collaboration.

Details of our award rates can be found in Annex 1.



Developing and commercialising 3Rs technologies through CRACK IT

CRACK IT is the NC3Rs open innovation programme which focuses on fostering 3Rs collaborations between big business and the SME and academic sectors.

It includes the challenge-led R&D competition CRACK IT Challenges and the technology partnering hub CRACK IT Solutions. In 2016 we introduced a new governance process for CRACK IT which included the establishment of an advisory panel.

The panel has a range of functions which include helping to optimise the commercialisation of products and services emerging from CRACK IT Challenges so that the full 3Rs benefits are realised.

Nine of the Challenges that have been funded since 2011 have now been completed. Of these, eight have delivered a product for further characterisation and validation, and five have a product that is already commercially available. This includes a new home cage monitoring system for rats and mice that can track a range of behaviours in animals group housed in their home cage. The first publications reporting use of the system were published in 2016 providing unique insights into the effects of genetic background on individual and group behaviour.

CRACK IT Challenges

In total there were seven Sponsors for the Challenges, one from the academic sector, four pharmaceutical companies and two agrochemical companies.

The EPSRC also provided co-funding to support two Challenges. A list of the Challenges and Sponsors can be found in Annex 2.

Of the four Challenges, two are what we refer to as two phase Challenges. The Challenge deliverables are broken down into six month phase 1 proof-of-concept studies where up to three £100k awards can be made, after which progress is assessed and one award is funded for phase 2. This second phase is typically for three years with up to £1 million available. In 2016, six phase 1 awards were made. Funding for phase 2 will be decided in July 2017. A list of contractors for phase 1 can be found in Annex 2. There were two Challenges which we refer to as single phase Challenges where awards of up to £100k are available

for Challenges that do not require significant R&D to solve. These were EASE which was sponsored by MRC Harwell to develop an approach to improve the implantation of non-surgically transferred embryos in the generation of genetically modified mice, and Maximise sponsored by Dow AgroSciences and Syngenta to develop *in silico* approaches to predict acute oral, skin and eye irritation of agrochemical mixtures without using animals.

In 2016, phase 2 awards, totalling £1.5 million, were made for the two CRACK IT Challenges launched in the previous year. Awards were made to a team from Newcastle for the Metaboderm Challenge to better predict skin metabolism for personal care products and topically applied pharmaceuticals, and from Heidelberg in Germany for the InMutaGene Challenge to assess the safety of gene therapy products using human induced pluripotent stem cells. Full details of the Challenge Sponsors can be found in Annex 2.

CRACK IT Solutions

Nine new CRACK IT Solutions were added to the technology partnering hub during 2016 taking the total number of 3Rs technologies showcased to 40. The aim is to help technology developers, from the academic and SME sectors, to identify partners to further develop, validate or commercialise their technology. In 2016, 67% of the technologies on the CRACK IT Solutions hub were from SMEs and 33% from academia, with 32% coming from organisations outside of the UK.

Seed funding of up to £30k is available to support new collaborations identified through CRACK IT Solutions. In 2016, six awards were made including for collaborations on animal-free approaches for antibody production, a new portable assay for botulinum toxin, and moth larvae for screening antimicrobial drugs.

Improving the rigour and reproducibility of animal research

Tackling the often poor design, analysis and reporting of animal studies is a key component of promoting the reduction part of the 3Rs and ensuring that the appropriate and minimum number of animals are used and that findings truly add to the knowledge base.

In 2016, we primarily focused on the ARRIVE reporting guidelines and the recently launched online Experimental Design Assistant (the EDA). In addition, we held our second experimental design workshop in partnership with the MRC for panel members of grant awarding bodies. This was attended by around 70 delegates from Research Council panels and focused on raising awareness on the importance of good experimental design in research proposals.

ARRIVE guidelines

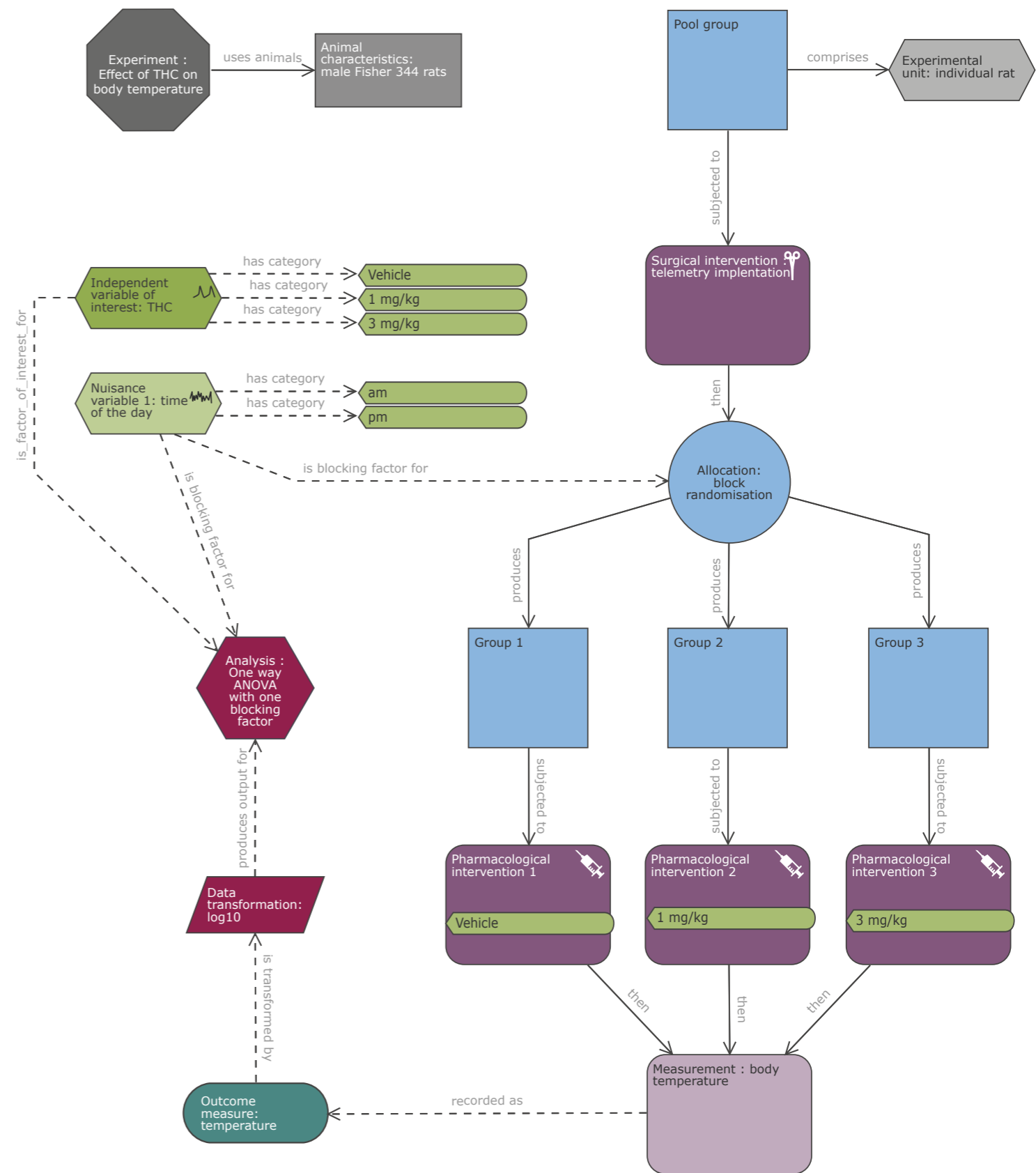
More than 1,000 scientific journals endorse the ARRIVE guidelines. In 2016 the entire Elsevier family of journals signed up to the guidelines. Enforcement by the journals supporting the ARRIVE guidelines is patchy and in practice many are not actively requiring manuscripts to include all of the items listed in the ARRIVE checklist. To help address this in 2016 we commissioned, in collaboration with the MRC, BBSRC and Wellcome Trust, a randomised

control trial to assess the impact of the ARRIVE guidelines on reporting quality with the aim of using the finding to inform any future revisions to the guidelines.

We continued to promote use of the ARRIVE guidelines across the scientific community. In 2016, we distributed more than 4,000 of the pocket-sized copies of the guidelines to 34 countries, adding the Japanese translation to the six other languages that the guidelines are available in.

Experimental Design Assistant

The EDA was launched in late 2015 and our focus for 2016 has been to raise awareness of this online tool that provides customised advice and feedback on experimental plans. During 2016, there were 2,178 users registered on the EDA and around 30 EDA 'diagrams' were created each week. The EDA was showcased in *Nature* in February 2016.



Supporting laboratory animal welfare

We have a large programme developing evidence-based refinements which improve laboratory animal welfare.

This is delivered through our research funding schemes and projects led by NC3Rs staff.

The programme focuses on a range of species and procedures and engaging a wide range of stakeholders. In 2016, we hosted our second joint symposium for animal care staff in collaboration with the Institute of Animal Technology. Topics on the agenda included automated home cage monitoring of mice, refining the husbandry of *Xenopus laevis*, and positive reinforcement training of pigs.

Non-human primates

Addressing concerns about the use of species of special concern to the public such as non-human primates continues to be a major part of our animal welfare programme. In 2016, we held our 13th annual primate welfare meeting which was sponsored by the Wellcome Trust and focused on the topical issue of cumulative severity.

In collaboration with the Yerkes National Primate Research Center at Emory University we conducted a survey on methods of training monkeys for chair restraint. This common procedure is potentially stressful for the monkeys yet little published information is available about its use and refinement.

The survey was completed by 101 laboratories worldwide and the results have been prepared for publication. Chair restraint formed the basis of a one-day practical workshop that we co-sponsored at the 2016 American Association for Laboratory Animal Science annual meeting in North Carolina.

A paper detailing the NC3Rs online resources for improving the care of non-human primates was published in the journal *Primate Biology*.

Rodents

Working with colleagues at the University of Liverpool we have published an online tutorial of refined mouse handling techniques. The video tutorial is based on the work we and the BBSRC have previously funded showing that picking mice up by the tail causes anxiety that affects welfare and scientific outcomes. In the first three months since its launch, the tutorial was viewed more than 2,000 times. The plan is to build on the tutorial, including with posters and practical training, to encourage the wider uptake of tunnel and cup handling which could affect the welfare of millions of mice worldwide.

In 2016, we published in the journal *Animals* a meeting report summarising the latest research findings on the welfare implications of different euthanasia methods for mice, rats and zebrafish. The report which includes recommendations to inform good practice for humane killing, received nearly 1,700 full-text downloads in the first six months following publication.

Fish

We hosted a three-day workshop with CEFAS on the welfare of laboratory fish. This included topics such as anaesthesia, euthanasia and welfare monitoring systems. A paper describing outputs of the workshop, as well as a survey of zebrafish users from 22 countries that we conducted, is being drafted for publication.

Welfare resources

To facilitate the uptake of refinements we have continued to provide a range of information resources and materials. In 2016, this included the launch of two scenario-based e-learning modules, aligned with the learning outcomes in the training framework established under Directive 2010/63/EU. The first is on recognising pain, suffering and distress in laboratory animals (mainly rodents), and the second is on the euthanasia of rodents and fish. The modules were funded through a previous NC3Rs Infrastructure for Impact award made to Professor Paul Flecknell at Newcastle University.

We have continued to promote our posters on recognising facial expressions of pain in the mouse, rat and rabbit. In 2016, we distributed almost 12,500 posters. These are available in English, French or Chinese. Almost half of those distributed were the Chinese translation.



Working with industry

We have a long-standing and wide collaboration with the pharmaceutical, biotechnology, chemical, agrochemical and personal care products industries.

This is supported, in part, by funding for two scientific posts from the ABPI¹ as well as funding from the chemicals sector²

The programme covers safety and toxicity testing and includes developing new 3Rs approaches and supporting changes in company practice and regulatory requirements. There are more than 70 companies and regulators involved in the NC3Rs industry programme from the UK, elsewhere in Europe, North America and Asia. In 2016, there were eight publications arising from the NC3Rs/industry collaboration. To further highlight our work, in September we hosted our first toxicology showcase event for 60 of our collaborators and stakeholders. We also organised sessions or presented our work at various international conferences including the International Congress of Toxicology in Mexico, the American College of Toxicology annual event in Baltimore and the Safety Pharmacology Society annual meeting in Vancouver.

Key highlights from the programme in 2016 include a new initiative with the pharmaceutical industry to review the use of second species

in regulatory toxicology studies focusing on the question of 'when would data from one species be sufficient for safe progression in humans?'; a publication reporting an NC3Rs-led project reviewing the utility of rodents in safety pharmacology studies for central nervous system endpoints, for predicting adverse events in humans; and the launch of a new cross-sector industry programme on exposure-based risk assessment.

Many of our industry projects focus on acting as an honest broker for cross-company data sharing to highlight opportunities for minimising animal use or suffering. In 2016, this included sharing information on the barriers to the uptake of the one concentration approach in fish bioaccumulation testing, analysis of the scientific value of *in vivo* testing for biosimilar mAb products, and reviewing the impact of social housing of non-human primates, minipigs and dogs on experimental data during telemetry recording of cardiovascular parameters.

Some of the data analyses we conduct are complex and highly detailed. This is illustrated by the work we have done to support OECD

acceptance of the fixed concentration procedure (FCP) for inhalation toxicity testing, a method that uses signs of evident toxicity rather than death of the animals as an endpoint, unlike existing OECD test guidelines. In 2016, our efforts to have the FCP accepted as an OECD test guideline were rejected at a meeting of representatives of member states. This was despite evidence provided from an analysis of an extensive dataset on 188 substances, with information on at least two different concentrations for each substance. Each concentration usually involved ten rats (five of each sex), which were exposed to the test substance for four hours and then monitored for clinical signs over 14 days. There were over 40 different clinical signs recorded and the dataset included around 4,500 animals in total.

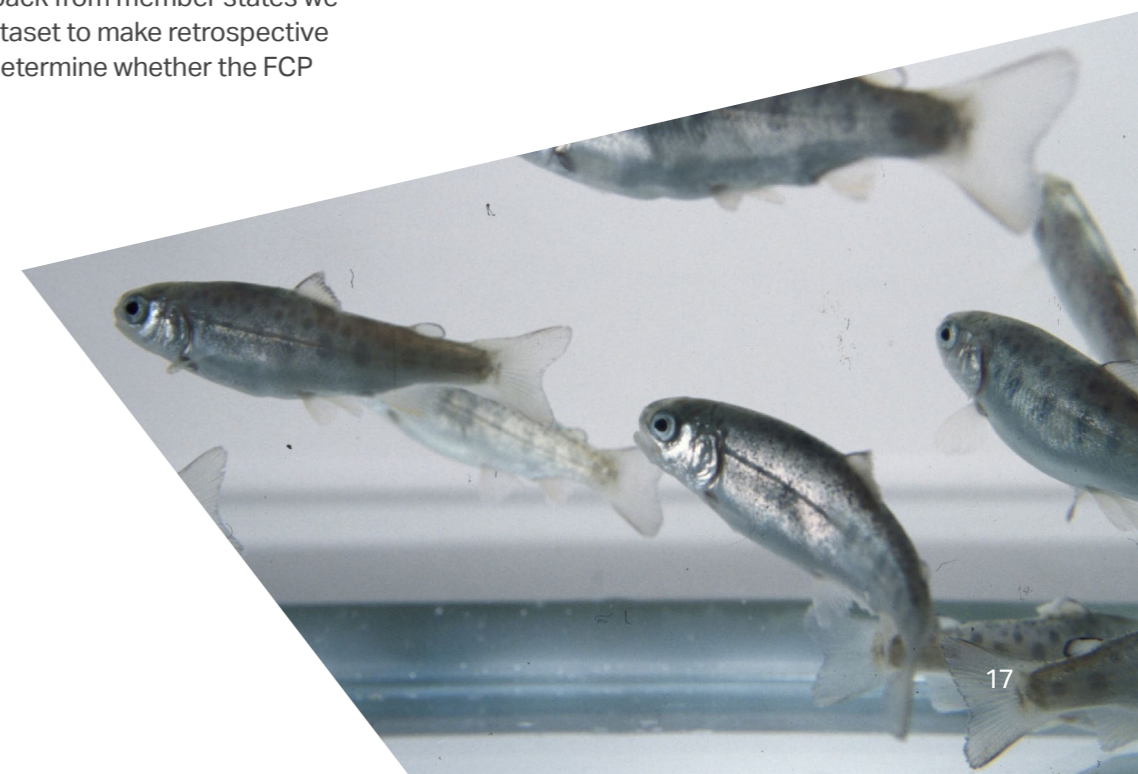
We conducted multiple analyses of the dataset to support the use of evident toxicity. This included investigating if signs observed at the lower concentration could predict death at the higher concentration, in various scenarios. We looked at the predictivity of individual clinical signs (including their severity and duration and the frequency observed) as well as the predictivity of a combination of signs. We also carried out analyses to examine the potential for the FCP to give false positives and false negatives results. Following the OECD decision and feedback from member states we re-analysed the dataset to make retrospective classifications to determine whether the FCP

provides the same chemical hazard classification as the existing OECD test guidelines with the aim of pushing for OECD acceptance in 2017.

As well as maximising 3Rs opportunities through data sharing we also support the development of new scientific approaches to safety testing. These primarily focus on replacing animal use. In 2016, we continued to build on our work on adverse outcome pathways (AOPs) for risk assessments, hosting a one-day workshop on how to use AOPs in practice. Aligned with this, we have also initiated a new project on exposure science as this is key in the transition to AOP-based approaches, where exposure considerations are essential for the interpretation of *in vitro* tests and understanding of how the concentrations of chemicals used in these tests relate to the potential real-life doses experienced by humans and other organisms in the environment. As first steps for the exposure project we have established a cross-sector working group to advise on our activities in this area, and are hosting a two-day workshop on applying exposure science to increase the utility of non-animal data in safety testing. The workshop is scheduled for early 2017 and is being organised in collaboration with Unilever.

¹Funding is coordinated by the Association of the British Pharmaceutical Industry (ABPI) with the following companies contributing: AstraZeneca plc, Covance Laboratories Ltd, GlaxoSmithKline plc, Eli Lilly & Company Ltd, Envigo, Novartis Pharmaceuticals Ltd, Pfizer Ltd, Shire Pharmaceutical Development Ltd, Takeda Cambridge Ltd, UCB Pharma Ltd.

²Unilever, Syngenta, Shell, Dow and SC Johnson.





Working with research funders

We have continued to build on our collaboration with the UK's major research funding bodies primarily through our 3Rs peer review of grant proposals.

Our peer review service is used by 17 research funders for 65 schemes, primarily focusing on applications which include the use of non-human primates, dogs, cats, pigs or equines and on occasions other species where large numbers of animals will be used or where there are novel or risky procedures involved.

In 2016, Cancer Research UK, Parkinson's UK and the Academy of Medical Sciences joined the service. During the year we reviewed a total of 128 applications, up 37% from 2015, with the increase largely accounted for by the inclusion of applications involving pigs at the request of the BBSRC. Of the applications reviewed, 30% were for work to be conducted overseas and 28% involved the use of non-human primates.

The NC3Rs peer review had a number of impacts including raising standards of husbandry and care for non-human primates and dogs in

institutes overseas, so that they are housed socially in enriched enclosures which meet the space allocations under Directive 2010/63/EU, and trained for cooperation with handling and procedures using positive reinforcement techniques.

Together with the Wellcome Trust and Science Europe, we organised a one-day workshop in Brussels on funding research involving animals. The event brought together 22 grant awarding organisations in Europe to share good practice in peer review and policy making to support high scientific and welfare standards in animal research. The funders agreed joint European funding principles for research with a focus on the 3Rs.

Disseminating advances in the 3Rs

We have a range of resources from newsletters to events to ensure there is wide dissemination and uptake of 3Rs methods and approaches.

Many of our resources are online. In addition to the main NC3Rs website, we also support four other microsites on topics from macaque welfare through to best practice for common procedures such as the administration of substances.

In 2016, the number of unique visitors to the NC3Rs website increased by 19% over the previous year from 245,452 to 301,361, with around 36% of traffic coming from the UK. The total number of visitors to all of the NC3Rs web resources increased by 21%, from 413,226 in 2015 to 522,298 in 2016. Content on all sites is regularly updated and in 2016 included a new monthly blog from the NC3Rs Chief Executive.

Social media and in particular Twitter is an increasingly important part of the NC3Rs communications strategy. In 2016, we reached 2,438 followers on Twitter, up 30% on the previous year. We continue to publish a monthly newsletter and in 2016 introduced a quarterly newsletter focusing specifically on toxicology.

In 2016, NC3Rs staff gave 106 presentations at national and international conferences. We also organised 14 events with more than 1,000 delegates attending. Events covered a wide range of themes, from a workshop in February on developing standards for non-animal technologies (organised jointly with Innovate UK, the British Standards Institute and the Stevenage Bioscience Catalyst), to a workshop in September on accelerating the use of mathematical modelling for safety assessment purposes (organised jointly with the US-based ILSI-HESI). A list of the NC3Rs events can be found in Annex 3.



Engaging the public in 3Rs issues

We have increased our focus on public outreach in 2016, maximising the interest from our grant holders and others in better providing opportunities to engage in the 3Rs.

In October, we hosted an event in collaboration with the British Library as part of their 'Talk Science' series which included presentations on the how and why animals are used, how the 3Rs are applied in the pharmaceutical industry and non-animal approaches to studying neurological and psychiatric disorders.

We continued to participate in the annual 'Pint of Science' event, sponsoring events in Southampton, London and Edinburgh.

To meet demand we have re-launched our public engagement awards which are available to current and previous NC3Rs grant holders.

Awards of up to £1,000 are available. In 2016, we made four awards for public engagement activities in Aberdeen, Glasgow, Swansea and Hull, including two awards to early career researchers. The activities included two stalls at local science festivals, a school visit with a lab tour and experiments, and a public lecture with practical demonstrations. All events were well attended and generated positive feedback from the audiences and from the participating researchers.

The NC3Rs is a member of the Concordat on Openness in Animal Research.

Annexes

Annex 1: Awards funded through response mode schemes

- Project grants
- Strategic awards
- PhD studentships
- David Sainsbury Fellowships
- Infrastructure for Impact
- Summary of award rates by scheme

Annex 2: Awards funded through CRACK IT Challenges

- 2015 CRACK IT Challenges: Phase 2 Awards
- 2016 CRACK IT Challenges: Phase 1 Awards
- 2016 CRACK IT Challenges: Single Phase Awards

Annex 3: Events organised by the NC3Rs in 2016



Annex 1:

Awards funded through response mode schemes

Project grants

Dr Helinor Johnston et al, Heriot-Watt University

Developing alternative models to evaluate the impact of nanomaterials on neutrophils during the stimulation and resolution of inflammation (£344,251)

Dr Timothy Chico et al, University of Sheffield

Developing a zebrafish model of neurovascular coupling (NVC) (£353,324)

Professor Anthony Chalmers et al, University of Glasgow

A 3D *in vitro* glioblastoma cell culture system for identification and evaluation of novel radiosensitisers reducing rodent xenograft studies (£374,332)

Dr Patricija van Oosten-Hawle et al, University of Leeds

Unravelling the mechanism of transcellular chaperone signalling in *C. elegans* (£354,456)

Dr Oliver Britton et al, University of Oxford

Inter-neuronal variability in human nociceptor electrophysiology: experimentally-driven computational study of response to drugs and channelopathies (£284,524)

Professor Andrew Tutt et al King's College London

Towards *in vitro* oncology trials: drug testing in cultured patient derived tumour organoid cultures (£360,915)

Dr Oliver Burman et al, University of Lincoln

Automated predictive welfare assessment in groups of fish (£314,015)

Strategic awards

Professor Alexander Thiele et al, Newcastle University

Improving biological integration of osseous and dermal tissues in macaque cranial implants (£214,565)

PhD studentships

Dr Adriana Tavares et al, University of Edinburgh

Standardisation of preclinical PET/CT protocols across multiple research centres (£90,000)

Professor Peter Diggle et al, Lancaster University

Developing a novel experimental design and analysis model for longitudinal animal studies with high-dimensional outcomes (£90,000)

Dr Abdulrahman Shams Nateri et al, University of Nottingham

Genetic screens in intestinal/colon organoid (mini-gut) culture using the CRISPR-Cas9 system (£90,000)

Dr Martin Welch et al, University of Cambridge

In vitro reconstitution of the polymicrobial community associated with cystic fibrosis (CF) airway infections (£90,000)

Professor Karen Kirkby et al, University of Manchester

Development of a biologically-relevant preclinical radiotherapy dosimetry phantom (£90,000)

Dr Robert Knight et al, King's College London

Identifying regulators of tissue regeneration by *in vivo* imaging in the zebrafish (£90,000)

Dr Reiko Tanaka et al, Imperial College London

In silico design and optimisation of novel host-directed therapies (£90,000)

Dr Federico Dajas-Bailador et al, University of Nottingham

Modeling central and peripheral nervous system connectivity using compartmentalised microfluidic systems (£90,000)

Dr Anna Grabowska et al, University of Nottingham

Application of a 3D hydrogel-based model to replace use of animals for passaging patient-derived xenografts (£90,000)

Professor Margaret Knowles et al, University of Leeds

Organoid and single cell models of bladder cancer (£90,000)

David Sainsbury Fellowships

Dr David Turner, University of Cambridge

The establishment of left-right asymmetry in mammalian development (£215,335)

Dr Maria Duque Correa, Wellcome Trust Sanger Institute

Intestinal organoids as a replacement strategy to unravel early host intestinal epithelia interactions with whipworms (£251,248)

Dr Riccardo Storchi, University of Manchester

Interrogating the mouse visual system by automated analysis of voluntary behaviour (£218,947)

Infrastructure for Impact

Professor Matthew Guille et al, University of Portsmouth

Reducing the use and refining the distribution of male *Xenopus* (£106,760)

Professor Maria Belvisi, Imperial College London

Human tissue models for lung disease (£404,661)

Professor Blanca Rodriguez et al, University of Oxford

In silico human-based methodologies for evaluation of drug cardiac safety and efficacy (£512,253)

Summary of award rates by scheme

Funding Scheme	Number of applications received	Number of awards	Award rate (%)
Project grants	74	11	15%
Strategic awards	136	15	11%
PhD studentships	46	10	22%
David Sainsbury Fellowships	68	14	21%
Infrastructure for Impact	53	12	23%

Annex 2:

Awards funded through CRACK IT Challenges

2015 CRACK IT Challenges: Phase 2 awards

Metaboderm

Sponsors: Dstl (also co-funder), GlaxoSmithKline and Unilever
Contractor: Professor Lyle Armstrong, Newcells Biotech Ltd (£800,000)

InMutaGene

Sponsors: GlaxoSmithKline and Novartis
Contractor: Dr Manfred Schmidt, GeneWerk GmbH (£699,837)

2016 CRACK IT Challenges: Phase 1 awards

Osteo-chip

Sponsors: GlaxoSmithKline. The EPSRC and Arthritis Research UK also provided co-funding to support this Challenge.
Contractor: Dr Astrid Bakker, Stichting VU: Vrije Universiteit Amsterdam – ACTA (£99,973)
 Professor Kenneth Dalgarno, Newcastle University (£96,672)
 Dr Deborah Mason, Cardiff University (£99,820)

Retinal 3D

Sponsors: Roche, Merck and Novartis
Contractor: Professor Michael Cheetham, University College London (£99,999)
 Professor Stefan Liebau, University of Tübingen (£99,982)
 Professor Majlinda Lako, Newcastle University (£99,982)

2016 CRACK IT Challenges: Phase 1 awards

EASE

Sponsors: MRC Harwell
Contractor: Dr Virginia Pensabene, University of Leeds (£99,928)

Maximise

Sponsors: Dow AgroSciences and Syngenta. The EPSRC also provided co-funding.
Contractor: Professor Jonathan Timmis, SimOmics Ltd (£97,743)

Annex 3:

Events organised by the NC3Rs in 2016

David Sainsbury Fellows Meeting

28 - 29 January, London

Annual meeting of David Sainsbury Fellows to provide training and development opportunities in the 3Rs as well as skills such as grant writing.

Non-Animal Technologies cohort meeting: Standards in non-animal technologies

4 - 5 February, London

A workshop, held jointly with Innovate UK, the British Standards Institute and the Stevenage Bioscience Catalyst, to explore how performance standards (for materials, manufacture and benchmarking) can accelerate the development and application of non-animal technologies.

Improving peer review of *in vivo* research proposals

7 March, London

A workshop, held jointly with the MRC, to support panel members assess the quality of the planned experimental design in grant proposals.

Addressing the need for refinement in laboratory fish

26 - 28 April, Weymouth

A workshop on the welfare of laboratory fish jointly organised by the NC3Rs and the Centre for Environment, Fisheries and Aquaculture Science (Cefas), with sponsorship from AstraZeneca.

Pathways-based approaches across the biosciences: Towards application in practice

28 April, London

A workshop to share cross-sector knowledge and experience of applying pathways-based approaches in practice to improve safety assessment processes and reduce reliance on animal models.

Recent advances in alternative approaches for safety assessment and regulatory perspective

19 May, London

A joint workshop organised by the NC3Rs and the UK's Interdepartmental Group on Health Risks from Chemicals aimed at UK regulatory risk assessors and government agency toxicologists.



Using microsampling to refine blood sampling procedures in industry and academia

5 July, London

A symposium to highlight the refinement and reduction potential of microsampling

NC3Rs PhD Student Summer School

20 - 22 July, York

An event focusing on training in the 3Rs and networking skills.

CRACK IT Challenges launch

8 September, London

An event to launch the 2016 Challenges and give potential applicants an opportunity to meet the Challenge Sponsors.

Accelerating the acceptance of mathematical models as evidence in safety and efficacy decision making

14 - 15 September, London

A workshop co-organised by the NC3Rs and the US-based Health and Environmental Sciences Institute (ILSI-HESI) on mathematical models to improve the predictivity of efficacy and safety testing of drugs and chemicals.

Animal Technicians' Symposium

22 September, London

A symposium jointly organised by the NC3Rs and the Institute of Animal Technology for animal care staff.

NC3Rs Toxicology Showcase Event

29 September, London

An event dedicated to showcasing the NC3Rs toxicology programme to its collaborators and funders.

Primate Welfare Meeting: Cumulative severity and lifetime experience of NHPs in research

10 October, London

The annual symposium on non-human primate welfare, sponsored by the Wellcome Trust.

Opportunities in non-mammalian models of asthma

12 December, London

A workshop to review the outputs and findings of the four awards made under the 2014 strategic awards on non-mammalian models of asthma.

Acronyms

3Rs

Replacement, reduction and refinement of animals in research

ABPI

Association of the British Pharmaceutical Industry

AMRC

Association of Medical Research Charities

BBSRC

Biotechnology and Biological Sciences Research Council

EPSRC

Engineering and Physical Sciences Research Council

ESP KTN

Electronics, Sensors and Photonics Knowledge Transfer Network

ICH

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

MHRA

Medicines and Healthcare products Regulatory Agency

MRC

Medical Research Council

NACWO

Named Animal Care and Welfare Officer

OECD

The Organisation for Economic Co-operation and Development

SME

Small and Medium-sized Enterprises

TSB

Technology Strategy Board

