



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

Research culture and the 3Rs

Dr Mark Prescott,
Director of Policy and Outreach

Dr Nathalie Percie du Sert,
Head of Experimental Design
and Reporting

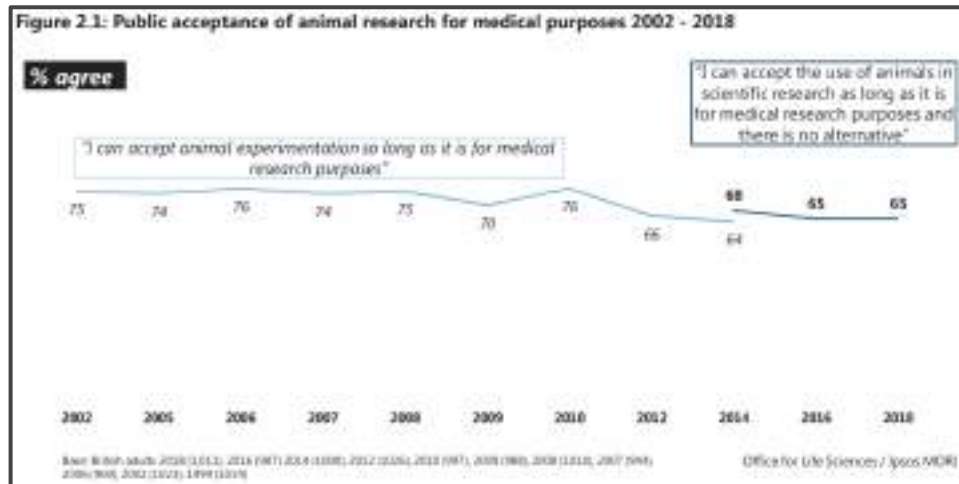
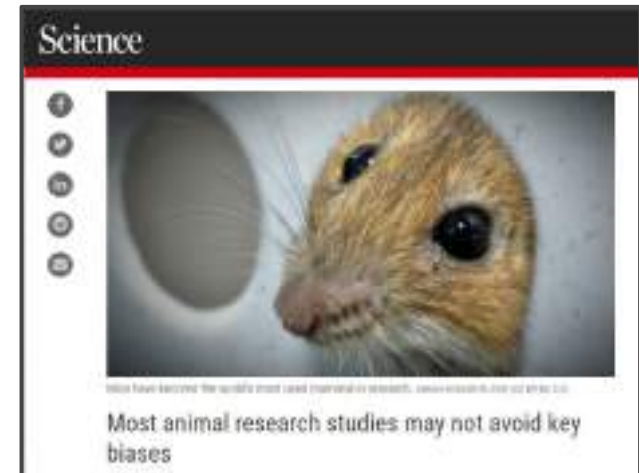
UKRIO Annual Conference, 20 May 2021

Animal use in research



A contentious issue

- Ethical issue of causing animals harm
- Falling levels of public support
- Concerns about poor experimental design and reproducibility
- Concerns about scientific validity and translation of animal models



MEDICAL NEWS TODAY

In mice: Are animal studies relevant to human health?

The media is rife with claims of breakthrough biomedical studies performed in animals. However, can animals ever faithfully model human health?

May 2019

Am J Transl Res 2014;6(2):114-118
www.ajtr.org/ISSN:1943-8141/AJTR1312010

Review Article

Lost in translation: animal models and clinical trials in cancer treatment

Isabella WY Mak^{1,2}, Nathan Everiew^{1,2}, Michelle Ghert^{1,2}

¹Department of Surgery, McMaster University, Hamilton, Ontario, Canada; ²Ajuntakki Cancer Centre, Hamilton Health Sciences, Hamilton, Ontario, Canada

The 3Rs – a framework for humane animal use

	Standard	Contemporary
Replacement	Methods which avoid or replace the use of animals	Accelerating the development and use of models and tools, based on the latest science and technologies, to address important scientific questions without the use of animals
Reduction	Methods which minimise the number of animals used per experiment	Appropriately designed and analysed animal experiments that are robust and reproducible, and truly add to the knowledge base
Refinement	Methods which minimise animal suffering and improve welfare	Advancing animal welfare research by exploiting the latest <i>in vivo</i> technologies and by improving understanding of the impact of welfare on scientific outcomes

The NC3Rs – headlines

- Established 2004 to accelerate the development and uptake of the 3Rs
- Research funder, plus in-house programmes led by NC3Rs staff
- Work with industry, academia, regulators and funders – not just UK, but also with collaborators in Europe, North America and Asia
- Remit includes any area of animal use for research purposes
- Team based in London, plus regional staff
- Budget ~ £10 million p.a.
- Independent Board



www.nc3rs.org.uk



Supporting changes in policy, practice and regulations

Our in-house programmes aim to overcome behavioural and cultural barriers that impede progress in the 3Rs

Challenges include:

- Poor awareness of 3Rs opportunities
- The rationale for change being poorly understood
- Endorsement of the 3Rs but limited change in practice
- Changes in practice not being rewarded in the current incentives structure
- Inertia (risk aversion, bar set too high)
- Lack of international standards



Research culture hub

Reliable, reproducible
and rigorous research



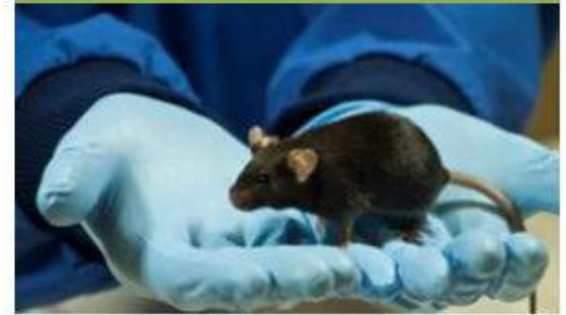
Our resources to encourage
high quality research.

Open research and
open communication



Communicating openly and
enabling open science
approaches.

Culture of care



Promoting responsible
animal research.

1. Reliable, reproducible and rigorous research
2. Open research and communication
3. Culture of care

Quality of animal research

In cancer science, many "discoveries" don't hold up

BY SHARON BEELEY

NEW YORK | Wed Mar 28, 2012 10:05pm EDT

30 COMMENTS | [Twitter](#) | [Facebook](#) | [LinkedIn](#) | [Share this](#) | [Print](#)

The Economist

World politics Business & finance Economics Science & technology Culture

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not

Oct 10th 2013 | From the print edition

[Timeskeeper](#)



Scientists told to stop wasting animal lives

Bad experiments for stroke and cancer drugs produce poor results, say research chiefs



Studies show only 10% of published science articles are reproducible. What is happening?

Posted on May 3, 2012 by Moshe Pritsker

Studies show a very low reproducibility for articles published in scientific journals, often as low as 10-30%. Here is a partial list:

REPLICATING RESULTS

Why Biomedical Research Has A Reproducibility Problem

February 26, 2014

TheScientist
EXPLORING LIFE. INSPIRING INNOVATION

NEWS & OPINION

MAGAZINE

Search

[Like](#) 48 [+1](#) 29

One of the fundamental principles of science is that a discovery is valid only if it can be reproduced. Without reproducibility, a scientific fact from error or a fluke from place to place and so on.

Home / Daily News

Preclinical Studies Don't Regularly Adhere to Best Practices

Animal experiments



Papers often don't state whether animals were randomized to control and treatment groups.

TheScientist
EXPLORING LIFE. INSPIRING INNOVATION

Home / Article / September 2013 / Op-eds

Fixing the Flaws in Animal Research

Many preclinical studies carried out in vivo are poorly designed and produce irreproducible data, but efforts to address the problem are



Sharon Kruse

REPRODUCIBILITY

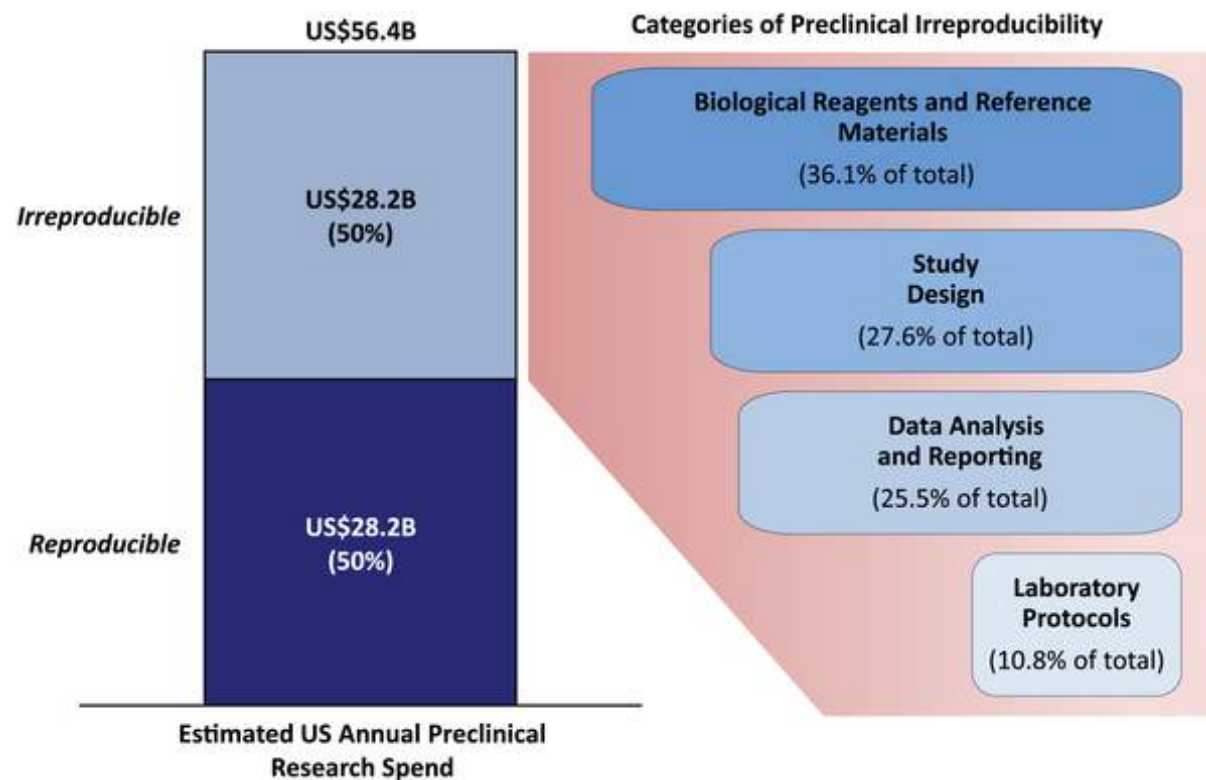
Sloppy reporting on animal studies proves hard to change

Scientists appear to ignore guidelines adopted 7 years ago

The Economics of Reproducibility in Preclinical Research

Leonard P. Freedman , Iain M. Cockburn, Timothy S. Simcoe

Published: June 9, 2015 • <https://doi.org/10.1371/journal.pbio.1002165>



50% of preclinical research wasted:

>1.6M animals per year wasted in the UK

Reproducibility and the harm-benefit analysis

If research is not reported in enough detail, or if findings are not reliable, benefits cannot be realised

→ Research is unethical

Likely benefits to science and society

- New scientific knowledge
- Improvements in human (or animal) health or safety



Likely harms to the animals involved

- Scientific procedures and their effects
- Contingent suffering due to housing, transport, etc.

Blinding



Elevated T-maze, dark arm reinforced

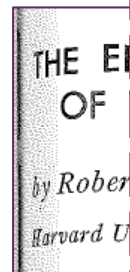
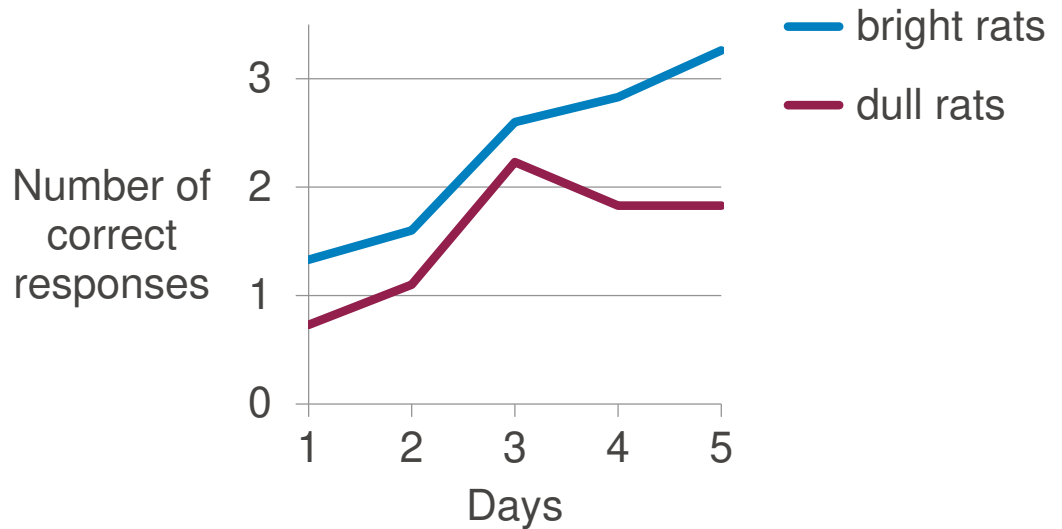
Two populations of rats:

- bright rats
- dull rats

12 researchers

NC
3R^s

Importance of rigorous design



- Rats had been labelled bright or dull randomly
- Only difference was in the minds of the researchers!

ANCE



Experimental Design Assistant (EDA)

Online tool for researchers to design *in vivo* experiments

Computer-based logical reasoning provides:

- Advice to improve the experimental plan
- Recommendations for the statistical analysis

Support for:

- Randomisation
- Blinding
- Power calculation

Improved transparency

EDA can help to ensure robust study design and reliable and reproducible findings

<https://eda.nc3rs.org.uk/>



The ARRIVE guidelines 2.0

A robust and collaborative effort

- International working group undertook the revision, 28 authors including:
 - Funders
 - Journal editors
 - Statisticians
 - Methodologists
 - Researchers from academia and industry
- Expert Delphi exercise – 73 participants from 19 countries
- Road testing of the guidelines and their explanation with researchers who publish animal research
- Compatible with and NIH reporting standards and many journals' policies



<https://arriveguidelines.org>

NC
3R^s



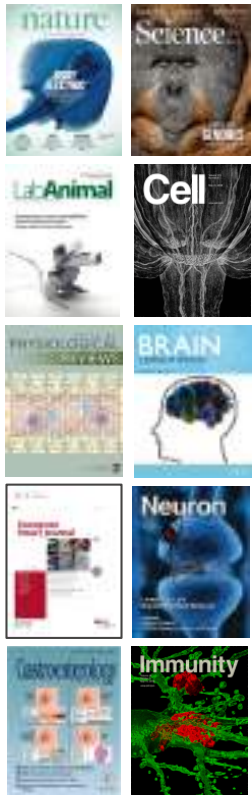
Impact of NC3Rs resources

Journals

Funders

Universities

Learned
Societies



1. Reliable, reproducible and rigorous research
2. Open research and communication
3. Culture of care

THE NC3Rs GATEWAY

This gateway promotes the sharing of science and technology funded by the NC3Rs



Read more in the blog →

Maximising the 3Rs impact of NC3Rs-funded research

This gateway provides a place for researchers funded by the NC3Rs to promote the 3Rs impact of their work, and publish rapidly, in an open and transparent manner.

The objective of the gateway is to raise awareness of new 3Rs

LATEST ARTICLES

The *in vitro* direct mycobacterial growth inhibition assay (MGIA) for the early evaluation of TB vaccine candidates and assessment of protective immunity: a

prot
Rach

Keep up to date with the NC3Rs



Transparency as a research funder



We are a signatory of DORA and actively apply its recommendations

We make information about our funding schemes publicly available, including:

- The assessment criteria for our grant schemes
- Success rates for the schemes
- Membership of our Funding Panels
- Diversity across our funding portfolio

Each award showcased on a dedicated webpage, summarising:

- Aims and key impact of the research
- Links to publications



Communicating with the public

- Our website includes public-facing information on the use of animals in research and the 3Rs

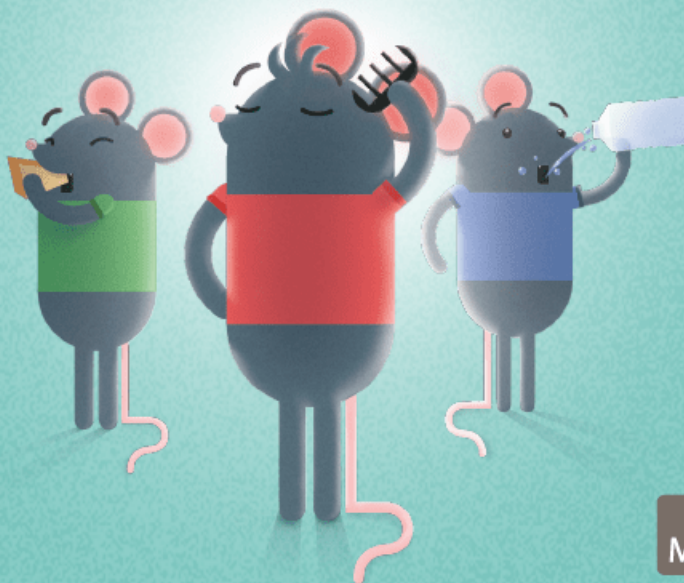
<https://nc3rs.org.uk/3rs-public>

- We offer awards to support NC3Rs-funded researchers to engage with the public
- We have sponsored events as part of the annual Pint of Science festival since 2014
- We are signatory on the Concordat on Openness on Animal Research



RODENT LITTLE BROTHER: SECRET LIVES OF MICE

BURROW INTO THE SECRET LIVES OF MICE TO HELP US ADVANCE MEDICAL RESEARCH AND MOUSE WELFARE



MRC

The
Mary Lyon Centre

NC
3R^s

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

RODENT LITTLE BROTHER: SECRET LIVES OF MICE STATISTICS

100% Complete

6,623

Volunteers

439,810

Classifications

42,387

Subjects

42,387

Completed Subjects

1. Reliable, reproducible and rigorous research
2. Open research and communication
3. Culture of care

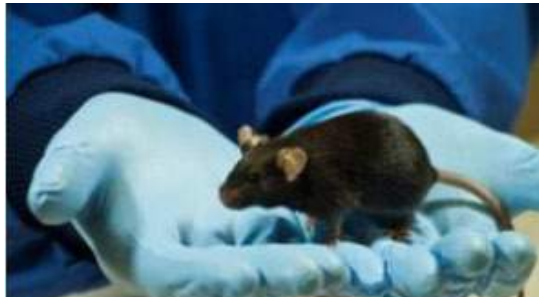
What is a culture of care?

“A healthy culture of care requires a shift away from merely responding to externally imposed standards, to one in which leaders and frontline staff actively commit to improving 3Rs, animal welfare and research, and working together to do so.”

Brown Report, 2013



Culture of care – responsibilities



In the animal house – refinement

- Utilising the latest research/technological developments
- Training and empowering staff
- Willingness to change practice



In the laboratory – rigour and standards

- Selecting the right model and design
- Reporting in a transparent and comprehensive manner
- Proactive engagement with the 3Rs




In the VC/registrar/dean's office – reputation

- Leadership – setting the standards and tone
- Fostering good team work and communication
- Being willing to say no

Resources to support culture of care

www.nc3rs.org.uk/3Rs-resources

Breeding and colony management



Guidance on re-establishing colonies after a pause (e.g. COVID-19 lockdown) with an emphasis on minimising the number of mice used.

Elsevier
Regulatory Toxicology and Pharmacology
journal homepage: www.elsevier.com/locate/yrtph

Opportunities for use of one species for longer-term toxicology testing during drug development: A cross-industry evaluation

Helen Prior^{a,*}, Paul Baldrick^b, Sonja Beken^c, Helen Booker^d, Nancy Bowen^e, Paul Brooker^f, Paul Brown^g, Brian Burlinson^h, Leigh Ann Burns-Naasⁱ, Warren Casey^j, Melissa Chapman^k, David Clarke^l, Lefke de Haan^m, Olaf Doehleⁿ, Noel Downes^o, Meghan Flaherty^p, Nicholas Gollaty^q, Sophia Gry Moesgaard^r, Jennifer Harris^s, Mark Holbrook^t, Julia Hu^u, David Jones^v, Keith Jones^w, Hille Kerdin^x, Andreas Mahl^y, Alf Manninen^z, Aidan McGuire^{aa}, Elisabeth Mortimer-Casson^{ab}, Marjorie Peraza^{ac}, Michael K. Piguley^{ad}, Jacques Richard^{ae}, Rath Roberts^{af}, Wendy Rooser^{ag}, Andresa Rothfuss^{ah}, Ankie Schoonmaker^{ai}, Fiona Sewell^{aj}, Richard Werner^{ak}, Lucinda Weir^{al}, Alison Wolfreys^{am}, Jan Kimber^{an}

NC 3Rs
Tech3Rs

Tickling rats for improved welfare

Alongside light and sound, tickling is a novel stimulus that can be used to improve the welfare of laboratory rats.

The Mammal Welfare

Guidance on re-establishing colonies after a pause (e.g. COVID-19 lockdown) with an emphasis on minimising the number of mice used.

NC 3Rs
The Rabbit Grimace Scale

	Without a score	Score of 1	Score of 2
Head position	[Image]	[Image]	[Image]
Head movement	[Image]	[Image]	[Image]
Head position	[Image]	[Image]	[Image]
Head movement	[Image]	[Image]	[Image]
Head position	[Image]	[Image]	[Image]
Head movement	[Image]	[Image]	[Image]

NC 3Rs
Choosing contractors for animal research: expectations of the major UK public funders

Drs Mark Prescott & Kathryn Owen, NC3Rs



Administration of Substances

A series of tutorials to assist research workers developing their skills in the administration of substances to laboratory animals.

These video tutorials aim to assist research workers to develop their skills in the administration of substances to laboratory rodents. They focus on the manual skills needed to carry out the different procedures humanely and efficiently, and on the need to handle animals carefully to reduce any distress caused by the procedure.

Training and CPD opportunities

www.nc3rs.org.uk/webinars

Refining rodent
stereotactic surgeries
(April 2021)



Amanda Novak (Edinburgh) presents advice on good surgical technique and refinements to incorporate into rodent stereotactic surgery procedures.

Efficient management of
genetically altered
mouse colonies (March
2021)



A joint NC3Rs/Mary Lyon Centre webinar on applying best practice to get the most out of the minimum number of animals.

Tickling rats for
improved welfare
(January 2021)



Dr Megan LaFollette (NA3RsC) presents rat tickling as a positive handling technique and provides guidance on putting it into practice.

Moving to the use of
animal-free antibodies
(July 2020)



Overview of the scientific and welfare benefits of moving to animal-free antibodies and affinity reagents, including EURL ECVAM recommendations.

REGISTER: Rat
playpens for improved
welfare (Wed 5 May)



The welfare benefits of playpens for laboratory rats and how to implement them in your facility.

www.nc3rs.org.uk/e-learning-resources

Welfare assessment
(EU 5)



How to recognise and prevent pain, suffering and distress in laboratory animals.

Euthanasia (EU 6)



Principles and techniques for humane killing of laboratory animals.

Anaesthesia for
minor procedures
(EU 20)



Ensuring best practice in anaesthesia for minor procedures.

Anaesthetic
monitoring and
intraoperative care
(EU21-3)



Why and how to monitor anaesthetised animals.

Anaesthetic
management and
preventing problems
(EU21-5)



Managing anaesthesia and what can be done to prevent problems.

The role of funders – policies and guidelines

Compliance with the principles in these three guidelines is a condition of research funding for many public funding bodies



Peer review and advice service

- We review all proposals involving NHPs, cats, dogs, equines and other species for 28 funding organisations internationally
- Our input enhances quality of science, animal welfare, and helps protect the funder's reputation
- Over 1,250 proposals reviewed since 2004 since; around 50% with animal use overseas



Direct support for research institutions

Regional Programme Managers



Dr Joanna Stanley
(North West & Yorkshire)



Dr Chris Barkus
(Oxford)



Dr Jessica Eddy
(Cardiff & South West)



Recruiting
(Midlands)



UNIVERSITY OF
BIRMINGHAM



UNIVERSITY OF
LEICESTER



The University of
Nottingham

UNITED KINGDOM • CHINA • MALAYSIA

Dr Ellen Forty
(London)



Vacant
(London)



3Rs advice for project licence applicants



Advice and resources to help applicants address the 3Rs aspects of a project licence application

Webpage and downloadable PDF

NC
3Rs

- Developed by the RPMs using their “on the ground” experience
- Highlights 3Rs resources available from the NC3Rs, as well as other organisations
- Includes advice on searching for replacement models, tips on experimental design and reporting, and links to help identify the latest refinements



nc3rs.org.uk/3rs-advice-project-licence-applicants

3Rs self-assessment tools



Free-to-use, secure online tools for tracking, evaluating and benchmarking your 3Rs activities and progress

<https://3rsselfassessment.nc3rs.org.uk>

NC
3Rs

The tools help research institutions and groups to:

- **Focus efforts** – scores can be used internally to allocate resources and concentrate discussions on the most important 3Rs areas
- **Track progress** – the self-assessment process can be repeated, and multiple scores logged over time, to see how 3Rs culture has developed
- **Find out what has worked before** – feedback gives advice and suggestions for improvement
- **Demonstrate commitment to the 3Rs** – users may wish to share their scores externally (e.g. grant proposal, PPL applications etc.)



3Rs self-assessment tools – feedback and advice



People: Suggestions for improvement

Consider strengthening your institution's 3Rs culture by.... For guidance, see the following...



- Fair Leadership: taking a strategic approach
- Fair People: ensuring the right culture
- Poor Research and infrastructure: supporting the best science
- Fair Experimental design and reporting: robust and reproducible studies
- Fair Training: building capability
- Poor Publications and wider dissemination: sharing impacts

Benefits of a good research culture

- Better, more efficient and impactful science
- Better animal welfare
- Better chance of public confidence
- Better workplace environment





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

Thank you!

For more information

-  mark.prescott@nc3rs.org.uk
-  nathalie.perciedusert@nc3rs.org.uk
-  www.nc3rs.org.uk
-  [@NC3Rs](https://twitter.com/NC3Rs)

Keep in touch

Our monthly newsletter provides the latest updates from the NC3Rs www.nc3rs.org.uk/register

Pioneering Better Science