Research culture and the 3Rs

Dr Mark Prescott,
Director of Policy and Outreach

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

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Animal use in research

Basic research

Chemical development

Drug development

Veterinary medicine
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
## The 3Rs – a framework for humane animal use

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<th>Standard</th>
<th>Contemporary</th>
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<td><strong>Replacement</strong></td>
<td>Methods which avoid or replace the use of animals</td>
<td>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</td>
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<td><strong>Reduction</strong></td>
<td>Methods which minimise the number of animals used per experiment</td>
<td>Appropriately designed and analysed animal experiments that are robust and reproducible, and truly add to the knowledge base</td>
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<td><strong>Refinement</strong></td>
<td>Methods which minimise animal suffering and improve welfare</td>
<td>Advancing animal welfare research by exploiting the latest <em>in vivo</em> technologies and by improving understanding of the impact of welfare on scientific outcomes</td>
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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.

https://nc3rs.org.uk/research-culture-and-3rs
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

Scientists told to stop wasting animal lives

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

Why Biomedical Research Has A Reproducibility Problem

Preclinical Studies Don't Regularly Adhere to Best Practices

Sloppy reporting on animal studies proves hard to change
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

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

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
Impact of NC3Rs resources
1. Reliable, reproducible and rigorous research

2. Open research and communication

3. Culture of care
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...
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

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
Training and CPD opportunities

- **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.

- **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.

www.nc3rs.org.uk/webinars  www.nc3rs.org.uk/e-learning-resources
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; around 50% with animal use overseas.

www.nc3rs.org.uk/peer-review
Direct support for research institutions

Regional Programme Managers

Dr Joanna Stanley (North West & Yorkshire)

Dr Chris Barkus (Oxford)

Dr Jessica Eddy (Cardiff & South West)

Dr Ellen Forty (London)

Vacant (London)

UNIVERSITY OF LIVERPOOL
MANCHESTER
The University of Manchester
UNIVERSITY OF OXFORD
University of Bath
University of Bristol
CARDIFF UNIVERSITY
UNIVERSITY OF EXETER

UNIVERSITY OF LONDON
LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE
THE FRANCIS CRICK INSTITUTE
KING'S COLLEGE LONDON

UNIVERSITY OF BIRMINGHAM
UNIVERSITY OF LEICESTER
The University of Nottingham

UNITED KINGDOM - CHINA - MALAYSIA
3Rs advice for project licence applicants

- 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
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.)

https://3rsselfassessment.nc3rs.org.uk
3Rs self-assessment tools – feedback and advice

People: Suggestions for improvement

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

Leadership: taking a strategic approach
People: ensuring the right culture
Research and infrastructure: supporting the best science
Experimental design and reporting: robust and reproducible studies
Training: building capability
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
Thank you!

For more information

✉️ mark.prescott@nc3rs.org.uk
✉️ nathalie.perciedusert@nc3rs.org.uk
📍 www.nc3rs.org.uk
🐦 @NC3Rs

Keep in touch

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

Pioneering Better Science