



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

NC3Rs PhD Studentships Webinar

Dr Jonathan Gabriel
Webinar, Tuesday 3 April

Overview

- NC3Rs PhD studentship scheme introduction
 - What we offer, the application process, and timeline
- Our remit and the 3Rs
- Assessment criteria used by the Studentship Assessment Panel
 - Quality of the proposed project
 - Potential impact on the 3Rs
 - Expertise and track record of the Supervisor, training and research environment
 - Strategic relevance to highlight notices (where appropriate)
- Examples of PhD Studentship awards
- Added value and support we provide during Studentship awards
- Useful resources

NC3Rs PhD studentship scheme

What we offer, the application process, and timeline.

PhD Studentships

To embed the 3Rs in the training of graduate scientists from a broad range of scientific backgrounds.

Applications from any area of medical, biological or veterinary research are within remit; those that integrate a range of disciplines or include an industrial partner are particularly encouraged.



Who can apply?

To apply, you must:

- **Be a UK based researcher** with a minimum of five years postdoctoral experience. Applicants with limited supervisory experience are encouraged to name a more experienced colleague as a co-supervisor.
- **Be based at an eligible organisation:** Any UK research establishment, including HEIs, IROs and RC Institutes.

What we offer:

- **Level of funding:** £90k over 3 years (£30k/annum) covering student stipend, fees and research costs.
- **Duration of funding:** 36 months
- **Timing:** Annual competition
- **Available budget for 2018:** £1.08 million. 12 awards available + up to 3 NC3Rs-BHF awards.

NC3Rs/BHF co-funded PhD Studentships

Why cardiovascular research?

- Large numbers of animals are used in basic, translational and applied cardiovascular research.
- Currently used models, including surgery and drug administration, can involve significant pain and suffering.
- Questions around the utility and predictivity of some animal models for human cardiovascular disease.

Aims of the joint NC3Rs/BHF PhD Studentships:

- To support greater application of the 3Rs in cardiovascular science.
- To train excellent early career researchers in the 3Rs.
- Longer term aim of supporting scientific discovery to benefit patients.

Highlight notice



SYSTEMATIC
Review Facility



Highlight notice for 2018

Systematic reviews

Background and aims:

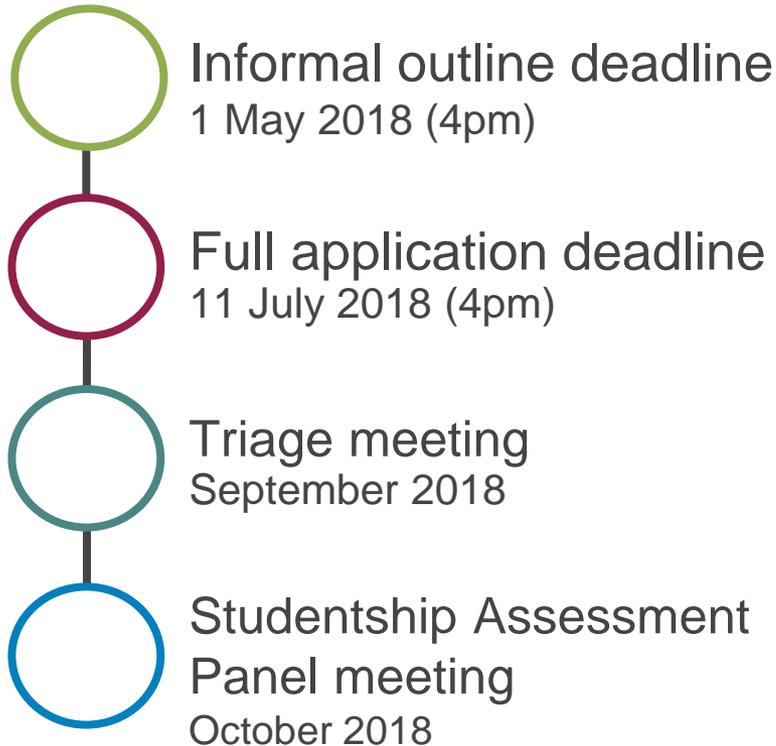
- Although systematic reviews are common practice in clinical research, they remain relatively under-utilised in animal research.
- Aim is to maximise their potential for advancing the 3Rs.

Process:

- Call for applications that incorporate systematic reviews within the proposed programme of work.
- Applicants are advised to contact the Office before submitting an application under this highlight notice.
- Guidance can be found on the [CAMARADES-NC3Rs Systematic Review Facility \(SyRF\)](#), and additional assistance is provided through the [web app](#), which is a free-to-use tool to help researchers perform systematic reviews and meta-analyses of animal studies.

Application process and timeline

Key dates 2018:



- Submit via email, assessed by the NC3Rs office for eligibility and remit.

- Shortlisted applicants will be invited to submit a full application via Je-S.
- No external peer review, applications will be assessed by the Studentship Assessment Panel.

- If a high volume of applications are received, a triage process will take place prior to the Panel meeting.

Our remit and the 3Rs

Our remit

Any area of science, technology, engineering or mathematics that has the potential to impact on the replacement, refinement or reduction of animals in research.

However...

Just because an application is technically within remit does not mean it will be competitive!

The primary driver of the proposal must be the 3Rs!

Definitions of the 3Rs

	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.

Replacement

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.



Potential replacement methods:

- Use of human tissue to investigate scientific questions.
- Use of new or existing *in vitro*, *in silico* or tissue engineered approaches.
- Use of invertebrate models such as *Drosophila* and *C. elegans* where there is a clear and direct replacement of vertebrate models.
- Use of non-protected immature forms of vertebrates such as embryonic and foetal forms.
- **NOT the replacement of one protected form with an another.**

Reduction



Appropriately designed and analysed animal experiments that are robust and reproducible, and truly add to the knowledge base.

Potential reduction methods:

- Advanced, novel imaging techniques for longitudinal studies instead of serial sacrifice – must offer novelty, not something that is already in routine use.
- Improved experimental design to allow more data to be gathered from the same animal.

Reduction approaches must not compromise the welfare of the animals used.

Refinement

Advancing animal welfare research by exploiting the latest *in vivo* technologies and by improving understanding of the impact of welfare on scientific outcomes.

Refinement refers specifically to improving the experience of the animal.

Potential refinement methods:

- Methods for assessing and improving animal welfare.
- Non-invasive or less painful methods.

Refinement research has to have the potential to deliver practical improvements in animal welfare, and cannot just be about understanding animal behaviour or sentience.



NC3Rs scoring matrix

- The Panel score on a 1 – 10 scale.
- Applications are scored using a matrix which considers both the 3Rs and the science and/or skills transfer.

SCIENCE AND TECHNOLOGY DEVELOPMENT	POTENTIAL 3Rs IMPACT				
	Exceptional	Excellent	Very Good	Good	Not competitive
Exceptional	10	9	8	7	5
Excellent	9	8	7	6	4
Very Good	8	7	6	5	3
Good	7	6	5	4	2
Not competitive	5	4	3	2	1

Assessment criteria used by the Studentship Assessment Panel

The following criteria are taken into consideration when making the funding decisions:

- Quality of the proposed project.
- Potential impact on the 3Rs.
- Expertise and track record of the Supervisor.
- The training / research environment.
- Strategic relevance to highlight notices (where appropriate).

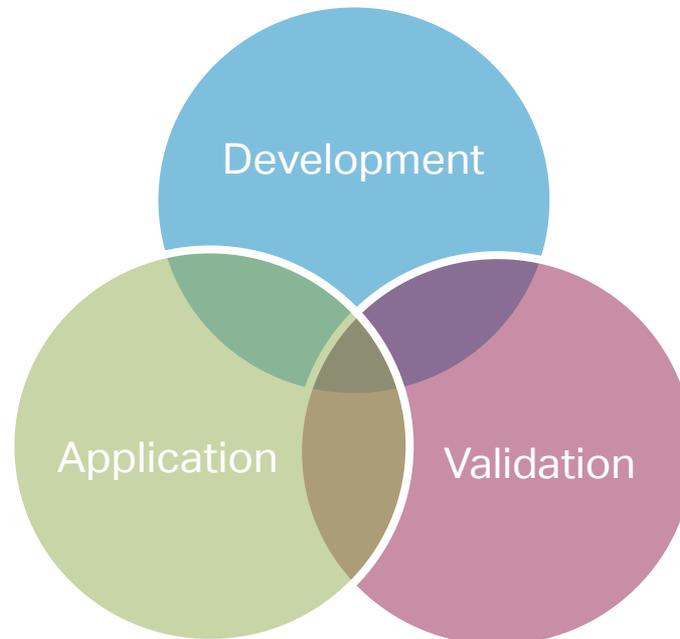
Quality of the proposed project

Quality of the proposed project

We are looking for projects based on excellent science that will deliver a practical change in the use of animals in research.

We are looking for applications that will challenge the “status quo” of the way things are done!

NC3Rs proposals should be focused on one of, or a combination of, these three aspects



Development

Applications may seek to develop a novel technology or method e.g. an *in vitro* assay, imaging approach or animal monitoring system.



Points that should be addressed:

- Recognise the competition
 - What similar methods already exist?
 - Scientifically, why is this approach significantly better?
 - What are some other benefits - is it more cost effective, or easier to adopt by other groups?
- Demonstrate feasibility - include preliminary or proof-of-concept data where possible.
- If developing a model using animal tissue, why would human tissue not be a suitable alternative at this stage?
- Have potential end users been engaged in the development process?

Validation

In order for a novel 3Rs approach to be adopted, it is important for the method to be validated, e.g. against the currently used state of the art approaches.



Points that should be addressed:

- What are the approaches currently used in the field and how will the new approaches be validated against these?
- Who are the potential end-users of the new method?
- Are there letters of support/ collaborations to demonstrate end-users would take it up?

Application

Using the new method to answer novel scientific questions **builds confidence** in and establishes the scientific benefits of the approach.

However...

Application of the method should be in the context of the 3Rs, and demonstrating the additional 3Rs benefits that can be achieved, and not simply about using the method.

Many proposals focused on application of a model often fall into the trap of focusing too much on the scientific outcomes and losing sight of the 3Rs objectives.

Points that should be addressed:

- How will application of the model encourage its adoption by others?
- What are the barriers to adoption and how can these be overcome? (e.g. access to human tissue/data/specialist equipment)
- Are there any additional steps necessary to support adoption of the model, e.g. regulatory changes, and have these been discussed?



Potential impact on the 3Rs

A well-articulated 3Rs case is crucial to success!

The 3Rs impact case

- **Which of the R's will the proposed research advance?**
- **How are you challenging the 'status quo'?**

Be specific:

- **What species of animal will be affected?**
 - Which species is currently used for this type of work?
 - Could the proposed method impact other species as well?
- **What type of animal procedures will the proposed research have an impact on?**
 - Will this affect all models, a certain model, or a specific aspect of a model?
 - Could it affect the severity limits of procedures / models?
 - Could it impact other similar models in use / research outside of your area?

3Rs metrics

We are looking for reasonable and realistic estimates based on a logical approach.

We are not looking for:

- Exaggerated numbers or sweeping statements.
- Broad generalisations, such as Home Office statistics.
- Arbitrary percentages / numbers - back your metrics up with logical workings.

We want to know the potential scale of 3Rs impact.

Metrics can be based on:

- How many animals are used locally for this work, and how many would be affected / no longer used.
- How many groups in the UK / overseas use the animal model and could benefit from the approach.
- How many papers published annually use this model, and how many animals are used in a typical publication.

Examples

BAD

According to the UK Home Office in 2014, 130,000 animals were used in basic oncology research and a further 60,000 in translational or applied human cancer research. The vast majority of the animals used in these procedures are mice. We believe our *in vitro* system can replace the use of mice in 20% of such research in the UK, equating to millions of animals worldwide.

GOOD

In our laboratory we use 1000 mice annually in this procedure which is classified as severe by the Home Office. Using our new method we can replace 50% of our animal work and use only 500 mice. We know of 5 other groups in the UK who use this model. Assuming they use a similar number of mice to us, our model could replace 3000 mice annually in the UK. A PubMed search shows there are 100 papers published each year that use the animal model. Each paper typically uses 200 animals. If our method was adopted we believe we could replace 50% of this use – equating to a further 10,000 mice internationally that would no longer be used in a severe procedure.

Leaving a 3Rs legacy

Maximum 3Rs impact can only be achieved if the method is adopted by others.

Points to address:

- What is the likely uptake of the 3Rs approach?
- Have you demonstrated buy-in from end-users and have you quantified what impact this would have on the 3Rs?
- What are the barriers to adoption and how can they be overcome? (regulatory, cost, technological, access issues, competition...)
- Is there a clear and reasonable dissemination plan?
 - It's not just about publications and conference attendance!

Routes to achieving impact:



Expertise and track record of the supervisor

Supervisory arrangements: Points for consideration

- Supervisory track record of the team:
 - How many previous students have completed their PhDs?
 - How many students do you currently have, and will the student receive an adequate level of supervision?
- Is there a co-supervisor that can balance any potential risk?
- Are contingency plans in place to ensure that the student will gain a PhD if difficulties are encountered with the work?
- Will this be a good training project for a student?
 - Is there a variety of techniques?
 - Will the student be able to develop parts of the project?
- What generic, scientific and specific 3Rs training will the student receive?

Expectations of 3Rs training

- 3Rs training activities should aim to increase engagement of the student with the 3Rs agenda and provide relevant learning, networking and /or dissemination opportunities.
- Examples could include, but are not limited to:
 - Lectures and other learning activities focusing on the relevance and impact of the 3Rs on scientific research, as well as current challenges.
 - Dissemination and discussion of 3Rs relevant research at 3Rs conferences/ symposia/ journal clubs.
 - Observation/ participation in 3Rs committees or AWERB meetings.
 - External outreach activities to lay audiences focusing on the 3Rs.

We want proposals to contain novel 3Rs training and engagement opportunities for our students.

Examples of PhD Studentship awards

Reduction and Replacement

3Rs approaches to assessing hepatotoxicity in drug development

- Hepatotoxicity is a major cause of drug attrition and drug-induced liver injury.
- Two methods for assessing liver toxicity developed:
 1. A novel zebrafish sampling methodology for blood based toxicity biomarkers which has resulted in the use of 63% fewer fish than the traditional methods.
 2. Transgenic zebrafish larvae containing fluorescent reporters under control of liver injury genes used to quantify the immune response to liver injury.
- James is now working with AstraZeneca to commercialize the model. Bastiaan's project also had a clinical element as it identified biomarkers for paracetamol overdose that can be used for patient stratification in hospital. James has partnered with Qiagen to develop this test as a diagnostic tool for A&E departments.

NC
3R^s



Dr James Dear and
Dr Bastiaan
Vliegthart



THE UNIVERSITY
of EDINBURGH

Refinement

Taming anxiety and variation in laboratory mice

- Methods of handling lab animals influence their physiology and behavior affecting welfare and introducing variability between animals.
- Kelly established a refined handling technique involving picking mice up with a small tunnel rather than tail.
- This avoids aversion and high anxiety behaviours shown by mice picked up by the tail, and also improves reliability of performance on cognitive behavioural tests.
- The team have taught the new technique to a wide range of groups, and collaborated with research organisations and industry to explore implementing improved handling as standard practice.



Professor Jane Hurst and
Dr Kelly Gouveia

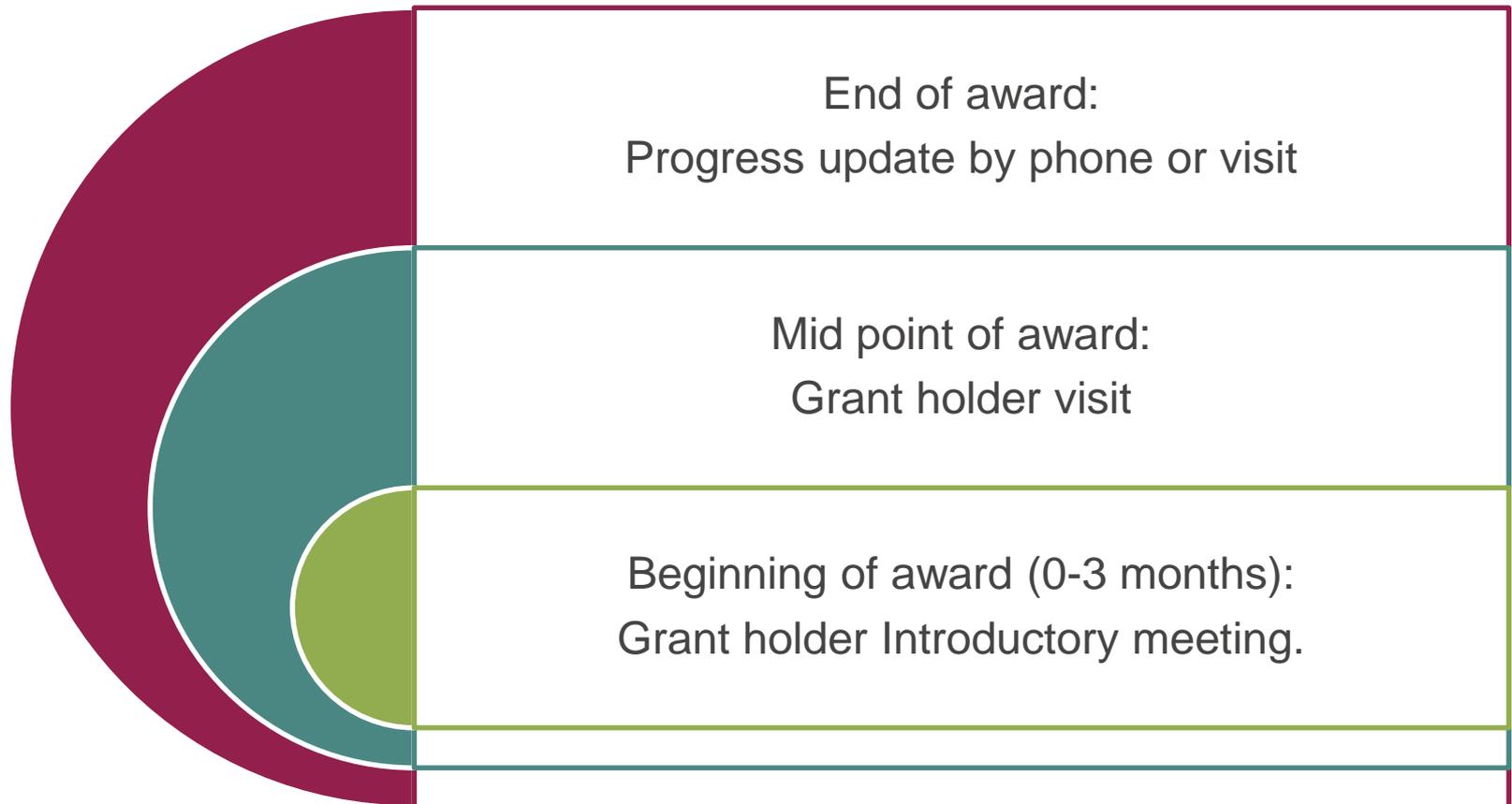


THE UNIVERSITY
of LIVERPOOL

Added value from the NC3Rs

Added value and grant holder interactions

At NC3Rs we are keen on nurturing our students and providing added value and support to our grant holders throughout the award



Communicating your research: NC3Rs channels

- News and press releases
- Blogs
- Newsletters
- Events
- Social media:

 Twitter @NC3Rs

 Facebook

 LinkedIn

Latest news



Reducing the use of male Xenopus frogs

Researchers at University of Portsmouth have optimised a robust sperm preservation method that will reduce the number of frogs used in research.



Announcing our new Skills and Knowledge Transfer grants

Four projects receive funding for the adoption of 3Rs approaches.



Maximising the success of bile duct cannulation studies

New recommendations for refining the surgical preparation of rats for bile duct cannulation studies.

Latest blogs



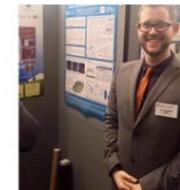
Guidance for university web pages on the 3Rs in animal research

Helping universities to demonstrate how they apply the 3Rs to their research.



Funding for PhD studentships in cardiovascular research

This year we have funding for three PhD studentships as part of our collaboration with the British Heart Foundation.



STEM for Britain: researchers visit the Parliament

NC3Rs-funded PhD student Neal Rimmer shares his experience of participating in STEM for Britain, a competition for early career researchers to present their work in the House of Commons.

NC3Rs events

- Grant holder introductory meeting
- International 3Rs prize event
- 3Rs symposia
- PhD Summer school

Home > Events >

2017 Primate Welfare Meeting

Central London
Registration deadline: Friday 13 October 2017 17:00

Subscribe to our newsletter

Get the latest articles, events and funding opportunities from the NC3Rs in your email inbox every month.

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Calendar of events

September 2017						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
27	28	29	30	31	1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

Sep 01

2017

NC3Rs

NC3Rs/BBSRC Workshop on Ageing Research

Central London

The NC3Rs and BBSRC are collaborating on a joint funding highlight notice to encourage the development of...

Sep 06

2017

Other

Planning and implementing the 3Rs: Strengths, weaknesses, opportunities and threats

South of England

LASA 3Rs/UFAW Section Meeting The LASA 3Rs



PhD Studentship Summer School



The University of
Nottingham

UNITED KINGDOM • CHINA • MALAYSIA



UNIVERSITY
of York



UNIVERSITY OF
CAMBRIDGE



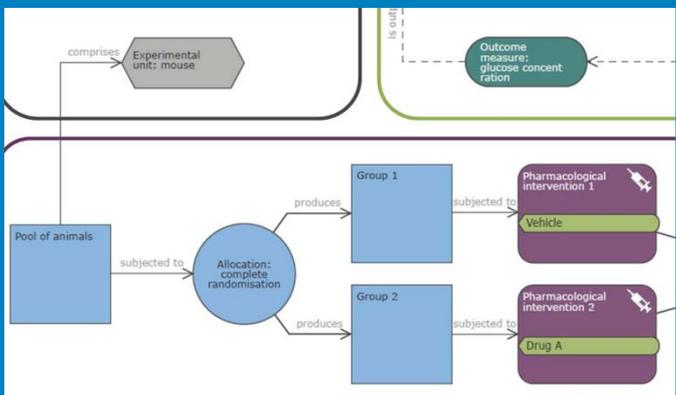
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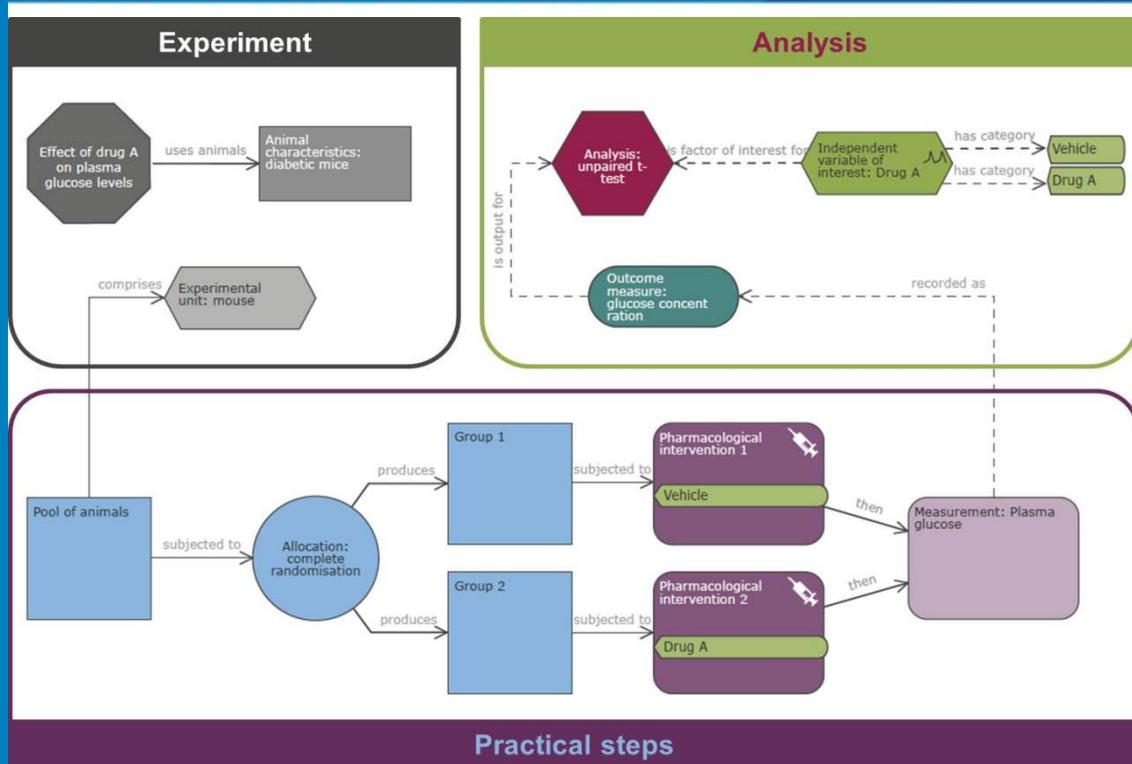
Useful resources

Experimental Design Assistant (EDA)

A new online tool for animal researchers to improve the design of their experiments.



- Consists of a web application and a supporting website.
- Can help to ensure robust study design and reliable and reproducible findings.



Benefits of the EDA include:

- Feedback and advice on your experimental design.
- Support for randomisation, blinding and sample size calculation.
- Practical information to improve knowledge of experimental design.
- Improved transparency, allowing you to share and discuss your plan with colleagues and collaborators.

Useful resources

Home > Funding

Funding

We are the main funder of 3Rs research in the UK with over £50 million to support projects

Open calls

PhD Studentships
Submission date: 12/07/2017
 The application form for invited...

NC3Rs Funding Schemes
 Applicant and Grant Holder Handbook

How to make a successful grant application

Related documents

Application Process

- NC3Rs Applicant and Grant Hold...
- MRC Guidance for Applicants an...
- Studentship application - commo...
- Notes and FAQs

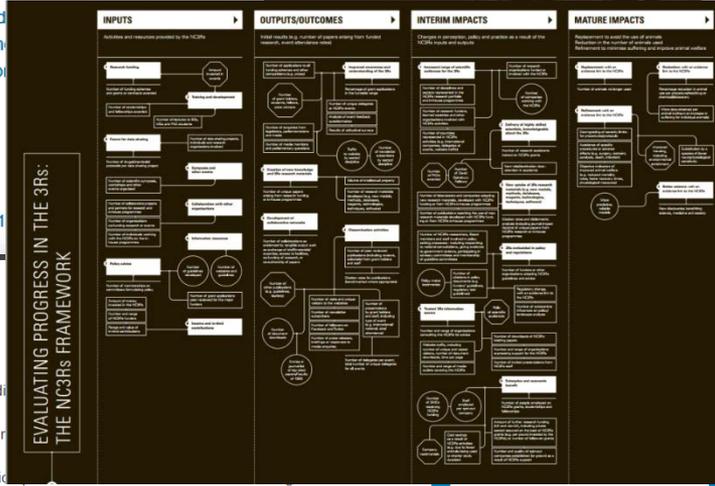
Forms

- Outline form 2017
- Supporting Information Form 201...
- Annex 1

Home > Our science

Our science

- Our science programmes are d...
- Research we fund through gr...
- CRACK IT our open innovati...
- Office-led activities headed by NC3Rs staff which focus on facilitating data sharing and knowledge exchange, developing evidence-based changes in policy, practice and regulations, and promoting the uptake of 3Rs approaches.



EDA
 Experimental Design Assistant

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 rom our

Eleven ways your funding application could be failing

Staff Blog
 Wednesday 29 March 2017



Tips from the NC3Rs funding team on avoiding common pitfalls when writing a grant application.



Search



National Centre
for the Replacement
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Further information – we're here to help!

Email: Studentships@nc3rs.org.uk

Website: www.nc3rs.org.uk

Keep in touch!

Our monthly newsletter provides the latest updates from the NC3Rs, including funding calls and events

www.nc3rs.org.uk/user/register

