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

Submitting a competitive NC3Rs grant application

Pioneering Better Science

Aims of this presentation

- We have seen an increase in demand for all of our funding schemes over recent years.

- We want to help potential applicants put in the strongest applications possible, by firstly determining whether their project is likely to be competitive and secondly what factors they need to consider when preparing the application.

- The NC3Rs funds across the full spectrum of science and technology, but the underlying focus must be on the 3Rs. This presentation concentrates on incorporating the 3Rs into applications.

- It will not cover policy and process issues already set-out in our Applicant and Grant Holder Handbook.

- This presentation is here for guidance and doesn't aim to cover all eventualities. If you would like to discuss a potential application we are always willing to help. Email: 3rsgrants@nc3rs.org.uk.

NC 3Rˢ

What is within the NC3Rs remit?

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. If the primary driver of the proposal is not the 3Rs consider a more appropriate funder.

Replacement

Methods that avoid or replace the use of animals defined as 'protected' under the (ASPA) in an experiment *where they would have otherwise been used.*

It is not replacement if your model will be used in a context where animals would not have been used anyway – e.g. due to cost or practicalities of using a large number of animals.

Potential replacement methods include:
- Use of invertebrate models such as *Drosophila* and *C. elegans* where there is a clear and direct replacement of vertebrate models.
- Use of new or existing *in vitro* or tissue engineered approaches that enhances the replacement potential of these methods.
- Use of non-protected immature forms of vertebrates such as embryonic and foetal forms, NOT to replace one protected form with an another.

NC 3Rˢ
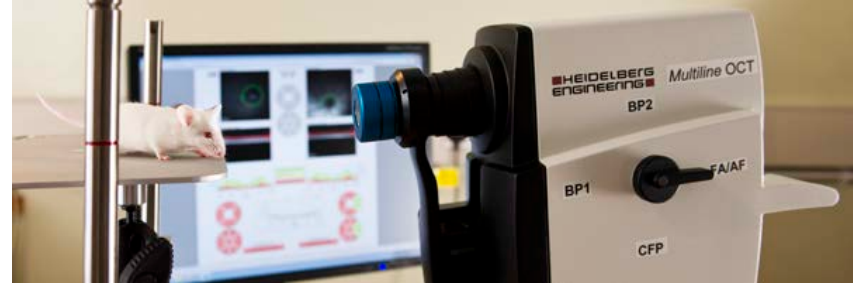
Reduction

Methods that minimise the number of animals used per experiment or study, either by obtaining comparable levels of information from fewer animals, or by obtaining more information from the same number of animals.

Potential reduction methods include:
- Imaging for longitudinal studies instead of serial sacrifice – however not something that is already in routine use and must offer novelty.
- Improved experimental design to allow more measures from the same animal .

NC
3Rˢ

Refinement

Methods that minimise the pain, suffering, distress or lasting harm that may be experienced by the animals. Applies to all aspects of animal use, from the housing and husbandry used, to the scientific procedures performed on them.

Refinement refers specifically to improving the experience of the animal.

Potential refinement methods include:
- 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 is not simply about understanding animal behaviour or sentience.

NC
3Rˢ
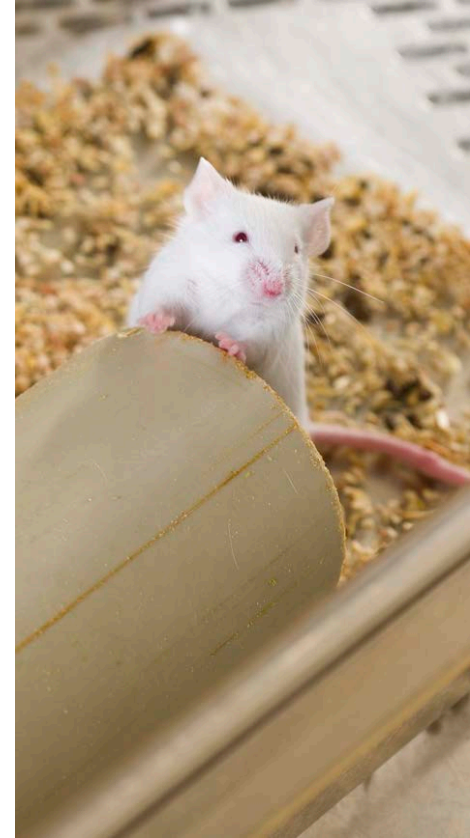
The remit in practice

All proposals need to offer a 3Rs impact. There needs to be a clear 3Rs legacy which demonstrates how a practical change in the use of animals in research will be achieved after the lifetime of the award.

We are looking for applications that will challenge the "status quo" and the way things are done.

In broad terms, proposals should be focused on development, validation or application of a 3Rs approach, or a combination of these three aspects.

Development

Application

Validation
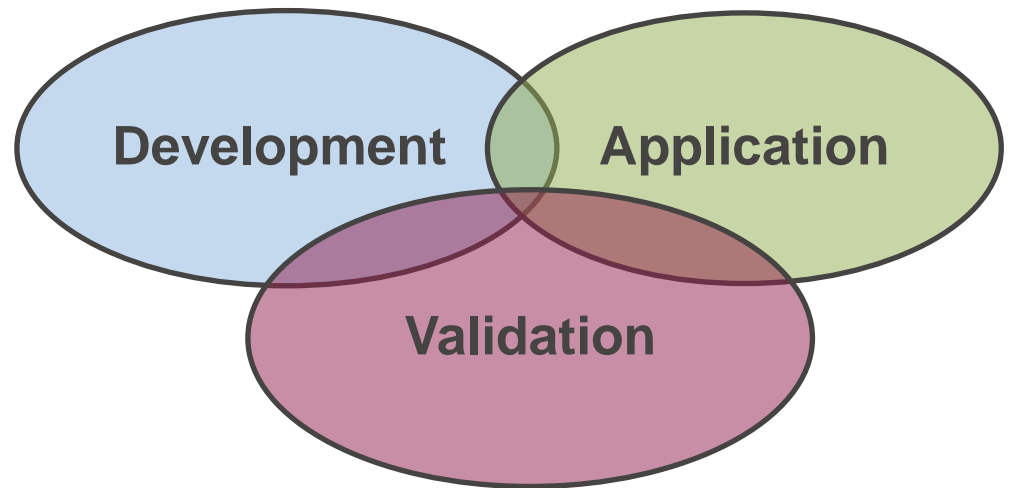
Development

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

The points to consider are:
- Recognise any competitors.
    - What similar methods already exist?
    - Why is your approach significantly better?
    - Does it offer additional 3Rs impact, is it more cost effective, or easier to adopt by other groups?
- Have you demonstrated feasibility? Include preliminary and proof-of-concept data in the application.
- If you will be developing a model using animal tissue why would human tissue not be a suitable alternative at this stage?
- Have you engaged the end users of existing models? Would they be interested in your alternative?

NC
3Rˢ

Validation

In order for a novel 3Rs approach to be adopted it is important for the method to be validated, e.g. against the current "gold standard".

The points to consider here are:

- What is the current "gold standard" in the field and how will you be validating against this model?
- Who are the end users of the existing models and do you have letters of support/collaboration to demonstrate they would use your method if it is validated?
- For *in vitro* techniques, have you engaged with the potential end users and those using the animal models you aim to replace?
- Would the method be relevant to industry users? If so, describe how.
- Are there any additional steps you can take to support adoption of the model, e.g. any regulatory changes?

Application

To establish the scientific benefits of a new 3Rs approach and to foster confidence, it is often necessary to answer novel scientific questions using the new method. Application of the method should however 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 down for focusing too far on the scientific outcomes and losing sight of the 3Rs objectives.

The points to consider here are:
- How will application of the model encourage its adoption by other users?
- What barriers to adoption are there and how can these be overcome – for example access to human tissue/data/specialist equipment?
- Is there a need to engage regulators and how will this be done?

NC
3Rˢ

How to demonstrate the 3Rs impact

A well-articulated 3Rs justification is crucial to success.
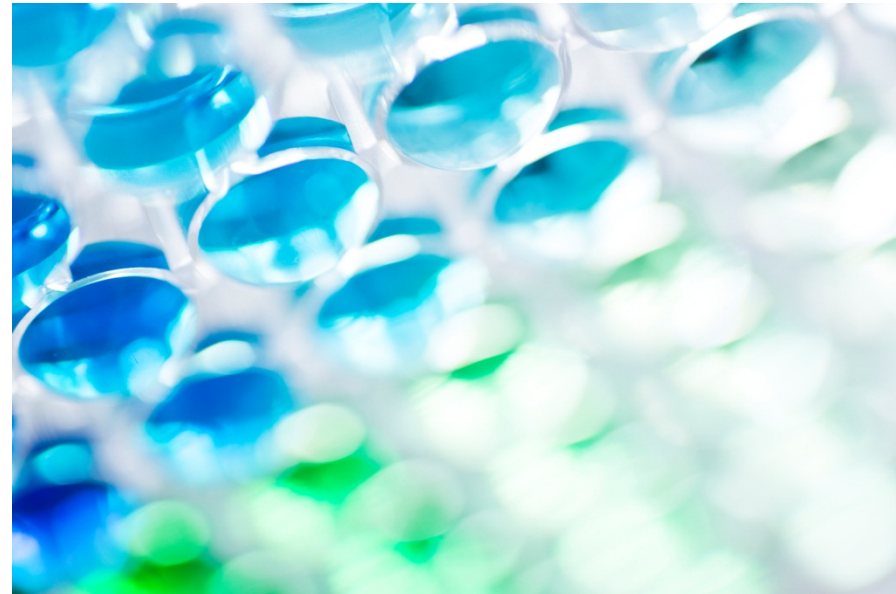
Be specific

- Which of the 3Rs will the proposed research advance?
  - Make sure you understand our [definitions](#)!
  - Just one "R" or potentially more?

- What species of animal will be affected?
  - Which species is currently used for this type of work?
  - Could the proposed method impact just this species or others? Just one or potentially more?

- What type of animal procedures will the proposed research have an impact on?
  - Will this affect all models, or a certain model, a specific aspect of a model?
  - Could it impact other similar models in use?

NC 3R

Provide metrics

The Panel will look at dozens of applications in any round and applicants have to make it clear as to why their proposal should be funded. Metrics on the numbers of animals that could be impacted are essential to this.

We are not looking for exact numbers for which you will be held to account – we are looking to see whether a concerted effort has been made to provide reasonable and realistic estimates based on a logical approach. Broad generalisations, such as Home Office statistics, are not helpful in the context of research impacting a specific model/field.

Consider:
- How many animals are used in your laboratory for this work annually, and how many animals would be affected/no longer used if successful?
- Approximately, how many groups are there in the UK/overseas that use the animal model and could benefit from your approach?
- How many papers are published annually that use this model? How many animals are used in a typical publication? How many animals is this per year? How much of this animal work could your method replace/reduce/refine?

NC
3Rˢ

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 believe 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.

NC
3Rˢ

How will you create a 3Rs legacy?

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

Consider:

- What is the likely uptake of the method?
- What are the barriers to adoption and how can they be overcome?
- Is there a clear and reasonable dissemination plan?
    - Publications are an expected output from all grants. However not just about publications – think outside the box.
    - Can you hold workshops to disseminate the method?
    - How will you teach people the methods? Website? Teaching workshops?
    - Is there anything the NC3Rs could help with?
    - Remember to cost in funds for dissemination activities!

Examples of dissemination from our Portfolio

Matt Leach validated the grimace scale for assessing post-operative pain in animals by looking at their facial expressions. With NC3Rs funding, the mouse and rat grimace scales have been produced as posters, with hundreds distributed worldwide.

Peter Jones developed an *in vitro* pseudoislet model for studying β-islet cells destruction during diabetes. With funding from NC3Rs, he held a two-day workshop attended by 10 different groups across Europe, to teach the method and build collaborations.

Ioanna Katsiadaki validated the use of the three-spined stickleback as a method for assessing endocrine disruption. She worked with the regulators at OECD to have the test adopted as an official test guideline.

NC 3Rˢ

General tips and advice

Science is as important as the 3Rs

- The Panel score on a 1 – 10 scale

- Applications are scored using a matrix which considers both the 3Rs and the science and/or technology development.

SCIENCE & TECHNOLOGY DEVELOPMENT	POTENTIAL 3Rs IMPACT				
	Exceptional	Excellent	Very Good	Good	Poor
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
Poor	5	4	3	2	1

NC 3Rˢ

Remember the 3Ps!
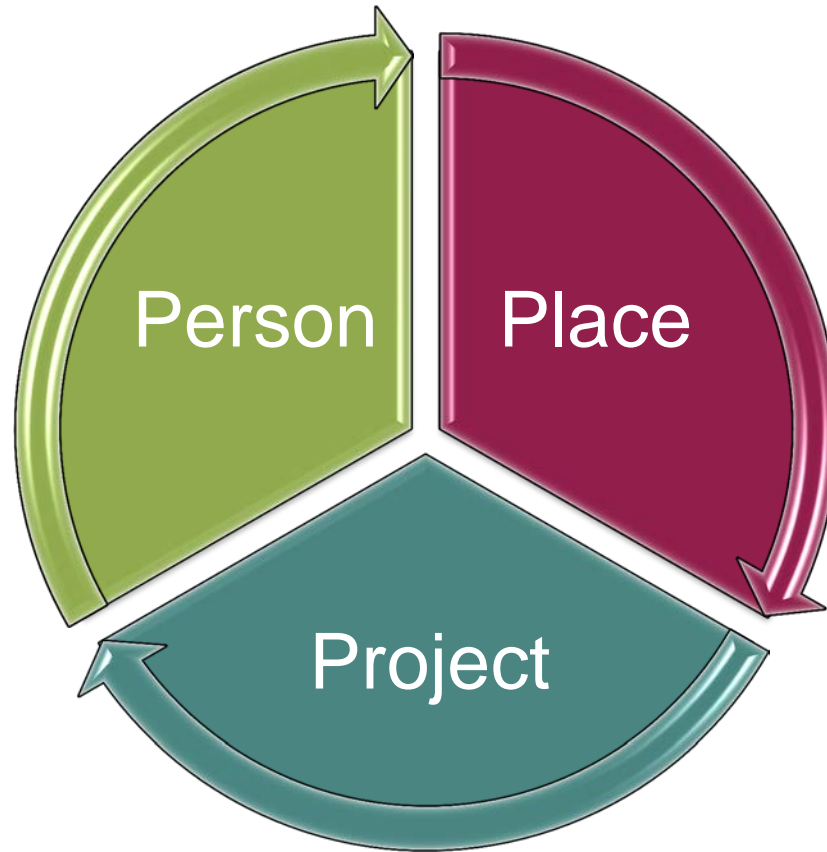
Person

The Panel need to have the confidence that the "team" can deliver the project.

- Expertise and track-record in the field.

  – Publications in the field.
  – Strengths and previous successes.
  – Examples of commitment to the 3Rs.

- Experience of co-investigators and collaborators.

  – Right balance of expertise and experience.
  – Can they bring anything additional to the team outside of the science? E.g. experience in the 3Rs, public engagement, industry experience?

NC 3Rˢ

Place

Is this the best place to do the work?

- Available facilities (access to specialised equipment, samples e.g. tissue bank).

- How will the institution support the research?

- Are there other researchers at the institution who will be able to support the project scientifically or in other ways?

- Will you have access to facilities outside of the host institute?

NC
3Rs

Project

Demonstrate robust science and the ability to deliver what you propose.

Consider:
- Is the project supported by preliminary or proof-of-concept data that demonstrates feasibility?
- Do you have knowledge of the field and recent developments - check what you are planning hasn't already been done and make sure you cite the competition and explain why your approach is better/adds value.
- Is the work feasible within the timeframe and resources requested?
- Have you considered the risks and do you have contingency plans?
- Is your experimental plan logical and detailed – it can't be assessed if it isn't included.

NC
3Rˢ

Use the form and attachments wisely!

- Makes sure your project title is clear, concise and relevant to the 3Rs.

- The lay summary will be made publicly available if awarded so make sure it is not overly technical and don't include sensitive information.

- Try not to repeat yourself – follow the guidance on what to include in each section.

- Include sufficient detail on the justification of animal numbers and experimental design, following the guidance in the [Applicant Handbook](#).

- The Pathways to Impact statement should not repeat the 3Rs information that is set out elsewhere in the application – think of the wider societal and economic impact of the work and the pathway to achieving this.

Scheme specific advice

Fellowships

- Consult the Fellowship specific guidance and use our [Skills and Experience Framework](#) to make sure you are at a competitive stage of your career for an award.

- Choose your sponsor and mentor wisely. Make sure they read your application and provide guidance on submitting a strong proposal.

- Will you be staying in the same laboratory/institution as your previous post? If so you must ensure you demonstrate independence:

    - State why this is the best place for the research.

    - How will you make sure you will be leading your own project and will not simply be "another pair of hands" in an established research group?

    - Will you be spending time in a different laboratory, e.g. in industry or with an overseas collaborator?

NC
3Rs

Studentships

- What is your supervisory track record? Have you had previous students who have completed a PhD? How many students do you currently have, and how will you ensure that the student receives an adequate level of supervision? Choose a co-supervisor that can balance any potential risk.

- Will this be a good training project for the student? Is there enough variety in techniques and will they be able to develop parts of the project?

- What contingency plans do you have in place to ensure that the student will gain a PhD if parts of the project do not deliver as originally planned?

- What generic, scientific and specific 3Rs training will the student receive?

Summary

- Why should the NC3Rs fund your proposal – could it be funded by another organisation?
- Is there a 3Rs legacy and have you made this clear in the proposal?
- Have you provided a well-articulated and reasoned 3Rs justification for the work including metrics?
- Is the project scientifically robust?
- How is the team and institution best positioned to deliver the project?
- If you are unsure or have questions contact the NC3Rs Office at 3rsgrants@nc3rs.org.uk