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

Peer Reviewer Guidance: Project grants

Thank you for agreeing to provide a review on an application for an NC3Rs Project grant. Balanced peer review comments are essential in assisting the Panel in making funding recommendations and your help in the decision-making process is much appreciated.

This document aims to provide information on the 3Rs, the Project grant scheme, specific guidance on completing your review on the Funding Service (TFS) and the scoring criteria. All information is shared in confidence, and you should destroy any files or printouts after use.

Please contact the Office at 3rsgrants@nc3rs.org.uk if you are unclear on any point or require further guidance. If you experience any problems with using TFS please direct queries to support@funding-service.ukri.org or call the helpline on +44 (0)1793 547 490.

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Background to the Project grant scheme

Project grants aim to support the development of new 3Rs approaches and technologies. Awards can be in any area of biological, medical, veterinary research or safety testing – those that integrate a range of disciplines or include an industrial partner are particularly encouraged. The amount requested should be dependent on the science and awards are for a maximum of three years.

Project grant applications are considered by the Grants Assessment Panel. Applications are invited from UK Higher Education Institutions (HEIs), Research Council Institutes and Independent Research Organisations (IROs, as described on the UKRI website).

The 3Rs

Submitted applications must fit within at least one of the 3Rs (Replacement, Reduction and Refinement). There is some variation in the exact interpretation of the definition of the 3Rs. The NC3Rs has adopted the following definitions:

Replacement

Replacement refers to technologies or approaches which directly replace or avoid the use of animals in experiments where they would otherwise have been used.

For many years research animals have been used to answer important scientific questions including those related to human health. Animal models are often costly and time-consuming and depending on the research question present scientific limitations, such as poor relevance to human biology. Alternative models can address some of these concerns. In the last decade or so, advances in science and technology have meant that there are now realistic opportunities to replace the use of animals. We divide replacement into two key categories, full and partial replacement.

- **Full replacement** avoids the use of any research animals. It includes the use of human volunteers, tissues and cells, mathematical and computer models, and established cell lines.
- **Partial replacement** includes the use of some animals that, based on current scientific thinking, are not considered capable of experiencing suffering. This includes invertebrates[1] such as *Drosophila*, nematode worms and social amoebae, and immature forms of vertebrates[2]. Partial replacement also includes the use of primary cells (and tissues) taken from animals killed solely for this purpose (i.e. not having been used in a scientific procedure that causes suffering).

Reduction

Reduction refers to methods that minimise the number of animals used per experiment or study consistent with the scientific aims. It is essential for reduction that studies with animals are appropriately designed and analysed to ensure robust and reproducible findings.

Reduction also includes methods which allow the information gathered per animal in an experiment to be maximised in order to reduce the use of additional animals. Examples of this include the use of some imaging modalities which allow longitudinal measurements in the same animal to be taken (rather than for example culling cohorts of animals at specific time points), or microsampling of blood, where small volumes enable repeat sampling in the same animal. In these scenarios, it is important to ensure that reducing the number of animals used is balanced against any additional suffering that might be caused by their repeated use.

Sharing data and resources (i.e. animals, tissues and equipment) between research groups and organisations can also contribute to reduction.

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[1] Note cephalopods such as octopuses and squid are protected in the UK by the Animals (Scientific Procedures) Act 1986.

[2] Under the UK's the Animals (Scientific Procedures) Act 1986 embryonic and foetal forms of mammals, birds and reptiles are protected during the last third of their gestation or incubation period, fish and amphibians once they can feed independently, and cephalopods at the point they hatch. Embryonic and foetal forms are protected from an earlier stage of development if they are going to live beyond the stage described above and the procedure is likely to cause them pain, suffering, distress or lasting harm after they have developed to that stage.

Refinement

Refinement refers to methods that minimise the pain, suffering, distress or lasting harm that may be experienced by research animals, and which improve their welfare. Refinement applies to all aspects of animal use, from their housing and husbandry to the scientific procedures performed on them. Examples of refinement include ensuring the animals are provided with housing that allows the expression of species-specific behaviours, using appropriate anaesthesia and analgesia to minimise pain, and training animals to cooperate with procedures to minimise any distress.

Evidence suggests that pain and suffering can alter an animal's behaviour, physiology and immunology. Such changes can lead to variation in experimental results that impairs both the reliability and repeatability of studies.

General guidance

Your assessment of the proposal should cover the following areas:

- **Vision of the project**
- **Approach to the project**
- **Capability of the applicants and the project team to deliver the proposed work**
- **Resources requested to deliver the project**
- **Ethical and responsible research and innovation considerations of the project**

Reviewers are also asked to consider other aspects of the research, including the potential impact and pathways to achieving this, ethical issues, appropriate use of animals, and data management plans.

There is no set way for answering questions on the form. However, Assessment Panels generally find the most useful reviews explicitly identify the main strengths and weaknesses in the proposal, while also giving a clear view on which should be accorded the greater significance and why. It is also helpful to raise issues or concerns with the proposal in the form of explicit questions for the applicants to address in their response. This aids the panel in assessing how complete and convincing the applicants' responses are.

It should be noted that anonymised reviews will be sent to the investigator (unless otherwise stated), who will be given the opportunity to comment on any specific queries raised.

Assessment criteria

When compiling your report, please use the following headings and guidance to aid your assessment. The detailed points outlined under each heading are intended as prompts, you do not need to address each of these in your report.

Vision of the project

When assessing the vision of the project, consider:

- Is there a need for research in this area? Is the proposed research scientifically original and innovative?
- Does the proposal address a strategically important 3Rs area/ question?
- Is the research of excellent quality and does it have importance within or beyond the field(s) or area(s)?
- To your knowledge, is the same or similar work being undertaken elsewhere?
- Does the proposal have the potential to advance current understanding, or generate new knowledge, thinking or discovery within or beyond the field or area?
- How timely is the research given current trends, context, and needs?
- Will the proposed research impact world-leading research, society, the economy, or the environment?
- Have the applicants identified the potential direct and indirect benefits of the research (particularly health, socioeconomic or environmental benefits) and who the beneficiaries might be?

Approach to the project

When assessing the proposed approach to the project, consider:

- Is the proposed approach effective and appropriate to achieve the scientific and 3Rs objectives?
- Is the approach feasible, and does it comprehensively identify any risks to delivery and how they will be managed? Are the plans to mitigate potential risks appropriate?
- Are the experimental plans clearly written and transparent?
- Have the applicants described relevant previous work and if relevant, how this will be built upon and progressed?
- Will the research directly replace, refine or reduce the use of animals in research/ testing? Is this clearly and convincingly explained?

- How widespread will the advance to the 3Rs be? Is it relevant to a specific area of work, or will it be implemented across a range of research areas?
- What is the likely scale of 3Rs impact (low, medium, high etc)? Are the supporting metrics realistic?
- What is the likelihood of success (i.e. replacing, refining or reducing the use of animals in research)?
- Will any additional steps be required before any advance in the 3Rs can be implemented?
- Is a dissemination strategy provided that outlines how the 3Rs outcomes of the project will be shared with the scientific community to encourage adoption by others (beyond attendance at scientific meetings and publications)? Are the plans appropriate and adequate?
- Are there any potential barriers to adoption by the wider scientific community that could limit the 3Rs impact?
- How will the team's research environment (in terms of the place and relevance to the project) contribute to the success of the work? Is there sufficient access to appropriate services, facilities, infrastructure, or equipment to deliver the project?
- Are collaborations well chosen? Have potential end-users been identified?
- Is the proposal likely to generate commercially exploitable results? If so, is the host institution adequately equipped to take forward the commercial development if any intellectual property may arise from the research and are the arrangements proposed appropriate?

Experimental design and methodology

Robust methodology and experimental design should be at the centre of any proposal to aid reproducibility of research findings. Consider whether the applicant has clearly described and justified the following:

- The hypotheses to be tested and high-level summary of the approach to be taken.
- Sample sizes to be used and supporting justification.
- Measures to reduce subjective bias (i.e. blinding or randomisation).
- Outcome measures that will be assessed and proposed analysis plans.
- Animals/ sample characteristics (i.e. sex, development stage, weight).

Capability of the applicants and the project team to deliver the proposed work.

When assessing the capability of the applicants and team to deliver the project, consider:

- Do the applicants and research team have relevant experience (appropriate to career stage) to deliver the proposed work?

- Is there the right balance of skills and expertise to cover the proposed work?
- Where applicable, does the applicants and research team have a track record in implementing the 3Rs in their research and disseminating research outputs and impacts?
- How well does the work fit with other relevant research pursued by the applicants?

Resources requested to deliver the project

When assessing the cost of the proposal and the allocation of resources, consider:

- Are the requested resources comprehensive and appropriate? Is there sufficient justification?
- Does the budget requested represent the optimal use of resources to achieve the intended outcomes?
- Is the number of staff appropriate for the work described? Have the applicants allocated time for and proposed an adequate level of involvement in the project?
- Will the requested resources maximise the potential outcomes and impacts?
- Does the proposal offer value for money?

Ethical and responsible research and innovation considerations of the project

For projects involving human participants, animal research and genetic and biological risks, please consider the following:

- Is the work ethically acceptable? Are there any ethical issues that need separate consideration?
- Are the ethical review and research governance arrangements clear and acceptable?
- Please consider if there are any ethical, safety or security issues, or other potential adverse consequences, associated with the proposed research.
- If applicable, is the use of animals justified in terms of need, species, number etc?
- Are there any tangible risks that the research would generate outcomes that could be misused for harmful purposes?
- Are there any actions which could lead to harm to humans, animals or the environment - including terrorist misuse?
- If such issues exist, have these been addressed satisfactorily in the proposal?

Overall assessment

You are asked to score the application using the scale below. The score should be a whole number between 1 – 6 where 1 is the lowest score and 6 is the highest. Decimals such as 0.5 are not allowed. The overall

score should reflect your overall view of the application. The following table is not intended to be prescriptive but should rather act as a general framework and guide.

Score indicators	Score
Exceptional quality **Science** ▪ Crucial scientific question or knowledge gap. ▪ Highly original and innovative; novel methodology and design. ▪ Of an international standard. ▪ Outstanding track record of the team and environment in this area. ▪ Ethical and/ or governance issues are fully considered. **3Rs impact** – Potentially very high, for example: ▪ Strategically important 3Rs area. ▪ Replacing/ reducing a large number of animals. ▪ Refining a severe procedure (even if numbers affected are low). ▪ Applicable to other models. ▪ Will have a local impact on animal use with a high likelihood of adoption by other groups nationally/ internationally.	**6**
Excellent quality **Science** ▪ Very important scientific question or knowledge gap. ▪ Original and innovative; novel methodology and design. ▪ Internationally competitive or leading edge nationally. ▪ Excellent track record of the team and environment in this area. ▪ Ethical and/ or governance issues are fully considered.	**5**

3Rs impact – Potentially high, for example: ▪ Strategically important 3Rs area. ▪ Replacing/ reducing a significant number of animals. ▪ Refining a severe/ moderate procedure (even if numbers affected are low). ▪ Could be applicable to other models. ▪ Will have a local impact on animal use with a good likelihood of adoption by other groups nationally/ internationally.	
<u>Very high quality</u> **Science** ▪ Important scientific question or knowledge gap. ▪ Robust methodology and design (innovative in parts). ▪ Internationally competitive in parts. ▪ Strong track record of the team and environment in this area. ▪ Ethical and/ or governance issues are fully considered. **3Rs impact** – Potentially medium/ high, for example: ▪ Addresses an important 3Rs concern. ▪ Replacing/ reducing a significant number of animals. ▪ Refining a moderate procedure (even if numbers affected are low) OR refining a mild procedure where numbers are high. ▪ Could be applicable to other models. ▪ Will have a local impact on animal use with the likelihood of adoption by other groups nationally/ internationally.	**4**
<u>Good quality</u> **Science** ▪ Worthwhile scientific question or knowledge gap. ▪ Methodologically sound study.	**3**

▪ Strong track record of the team and environment in this area. ▪ Nationally competitive. ▪ Ethical and/ or governance issues are well considered. **3Rs impact** – Potentially medium for example: ▪ Addresses an important 3Rs area. ▪ Replacing/ reducing a moderate number of animals. ▪ Refining a moderate procedure (even if numbers affected are low). ▪ Could be applicable to other models. ▪ Will have a local impact on animal use with potential for adoption by other groups.	
<u>Fair quality</u> **Science** ▪ Worthwhile scientific question or knowledge gap with potentially useful outcomes. ▪ Methodologically sound study but areas require revision. ▪ Appropriate track record of the team and environment in this area. ▪ Ethical and/ or governance issues are adequately considered. **3Rs impact** – Potentially low/ medium, for example: ▪ Addresses a 3Rs concern. ▪ Replacing/ reducing a low number of animals. ▪ Refining a mild/ unclassified procedure. ▪ Not applicable to other models. ▪ May have a local impact on animal use but unlikely to be adopted by other groups.	**2**

<u>Poor quality</u> **Science** ▪ Poorly defined questioned, flawed or duplicative. ▪ Not worthwhile. ▪ Methodologically weak study. ▪ Poor track record of the team and environment in this area. ▪ Ethical and/ or governance issues are not adequately considered. **3Rs impact** – no (or very low) 3Rs impact, for example: ▪ Does not address a 3Rs concern. ▪ Will not replace/ reduce any animal use. ▪ Does not refine a classified procedure. ▪ Not applicable to other models. ▪ Will not have a local impact on animal use or be adopted by other groups.	**1**
<u>Ineligible for funding</u> (For Office use only, NOT to be used by reviewer)	**0**