



Peer Reviewer Guidance: Project grants and Strategic awards

Please read carefully before completing the Je-S form. All papers are sent to you in confidence and you should destroy any files or printouts after use.

Thank you for agreeing to provide a review on an application for an NC3Rs Project grant or Strategic award. 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 funding schemes, specific guidance on completing the peer review form on Je-S and the scoring criteria.

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 the Je-S system please direct queries to the [Je-S Helpdesk](#).

1. Background to the Schemes

[Project grants](#) aim to support the development and application of the 3Rs. Awards can be in any area of biological, medical, veterinary research or safety testing and are for a maximum of three years. There is no maximum limit for the funds requested although they should be fully justified and commensurate with the research to be undertaken.

The [Strategic award](#) scheme provides funding opportunities in specific research areas identified as being strategically important to the Centre's goal of using the 3Rs to support science, innovation and animal welfare in the biosciences. The funding available and maximum duration of awards is dependent upon the call.

Project grant applications are considered by the [Grants Assessment Panel](#) and Strategic awards are considered by a bespoke Strategic award Panel. Applications are invited from UK Higher Education Institutions (HEIs), Research Council Institutes and Independent Research Organisations (IROs, as described on the [Research Councils UK website](#)).

2. 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 invertebrates¹ such as *Drosophila*, nematode worms and social amoebae, and immature forms of vertebrates². 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 (e.g. animals, tissues and equipment) between research groups and organisations can also contribute to reduction.

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.

3. General Guidance

The assessment of any research proposal submitted to the NC3Rs is based on four core criteria:

- 1. Importance: impact on the 3Rs**
 - 2. Scientific quality and potential: what are the prospects for good scientific progress?**
 - 3. Resources: are the funds requested reasonable and justified, and does the proposal represent good value for money?**
 - 4. Relevance to the NC3Rs strategy**
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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.

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, methodology and experimental design and data management plans.

There is no set way for answering questions on the form. However, Assessment Panels generally find reviews that 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, the most useful. 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.

4. Assessment criteria

In giving a written report on this proposal, please use the guidance below to decide the most appropriate section for your comments. The detailed issues given below under each heading are intended as prompts, but you do not need to address each of these in your report.

4.1 Reviewer Self-Assessment

Comments in this section will not be sent to the applicant but will be provided to the Assessment Panel.

Knowledge of the Applicant

Indicate briefly in what capacity you know the applicant(s) and their work. If there are any potential conflicts of interest, please contact the NC3Rs Office before reading the proposal. Examples of a conflict of interest include:

- Employed by the same institution as the applicant(s)
- Actively involved in research collaborations with the applicant(s)
- Working closely with the applicant(s), for example as a co-author or PhD Supervisor, or has worked closely in the last 5 years
- Holding a current position on the governing body of or an honorary position within the institution(s) of the applicant(s)
- In receipt of personal remuneration in excess of £5,000 per annum from the applicant's organisation
- Personal/family relationship with the applicant(s)

Your areas of expertise

Indicate briefly the areas of your expertise that are relevant to your assessment. Please indicate any areas of the proposal that you consider you are not qualified to assess, to enable the Office to select additional referees in these areas.

Other

Please indicate other potential conflicts of interests, such as if you have submitted a proposal to the same call for applications to the NC3Rs, or if there is significant overlap with ongoing work in your own laboratory. These criteria would not exclude you from reviewing the proposal, but should be noted.

4.2 Impact

Please consider the potential 3Rs impact of the project at the local, national and international level – both in the specific field and for the wider scientific community. Points for guidance include:

- Are the questions that are being addressed important 3Rs considerations?
- Will the research directly replace, refine or reduce the use of animals in research/testing?
- Is there a need for research in this area?
- What is the current and future importance of the techniques to medical, veterinary or biological research?
- What is the likelihood of success i.e. replacing, refining or reducing the use of animals in research?
- Does the proposal realistically set out the ultimate potential benefits with respect to the 3Rs?
- Will any additional steps be required before any advance in the 3Rs can be implemented?
- How timely is the work?
- Is there similar or complementary research underway elsewhere?
- How widespread will the advance in the 3Rs be? Is it relevant to a specific area of work, or will it be implemented across a range of research areas?
- Are there any potential barriers to adoption by the wider scientific community that could limit the 3Rs impact?
- What is the likely scale of the 3Rs impact (low, medium, high etc)?

4.3 Knowledge Transfer

The NC3Rs follows the [MRC policy on research data sharing](#) the underlying ethos of which is that publicly-funded research data are a public good, produced in the public interest and that they should be openly available to the maximum extent possible.

The NC3Rs expects valuable data arising from NC3Rs-funded research to be made available to the scientific community with as few restrictions as possible so as to maximize the value of the data for research and for 3Rs benefit. Such data must be shared in a timely and responsible manner.

In your review please consider whether adequate data sharing and knowledge transfer arrangements are in place as well as plans for commercial exploitation in particular:

- Is the proposed research likely to generate commercially exploitable results?
- Is the host institution adequately equipped to take forward the commercial development of any intellectual property arising from research and are the arrangements proposed in this case appropriate?

In addition:

- Have the applicants made any plans for public engagement or public understanding of science/3Rs in this proposal?
- Are these appropriate / sufficient?

- Is information provided about how the advances in the 3Rs will be disseminated over and above standard publications and presentations? Are these plans appropriate and adequate?

4.4 Proposal Assessment

ALL comments in this section will be sent, unedited, to the applicant. Your identity will not be revealed.

Scientific Potential

Please consider the following:

- What are the prospects for good scientific progress?
- Has the host Research Organisation demonstrated a commitment to supporting the work?
- Is there a firm foundation to take the work forward?
- Are collaborators well chosen?
- If this is a Strategic Award application, how well does the proposal address the aims of the call?

Research Plans

Please comment on the:

- Strength of the scientific case and how innovative the proposal is. To your knowledge, is the same or similar work being undertaken elsewhere?
- Robust methodology and experimental design should be at the centre of any proposal to aid reproducibility of research findings. Has the applicant clearly set out and justified the following:
 - Measures for avoidance of bias (eg blinding, randomisation)
 - Number of experimental and control groups and sample size per group
 - How the sample size was calculated, showing power calculations and including justification of effect size
 - Overview of the planned statistical analyses in relation to the primary outcomes to be assessed
 - Frequency of measurements/interventions to be used
 - Circumstances in which power calculations are not appropriate to determine sample size
- Identification of potential risks and appropriateness of plans to mitigate these.
- Immediacy of implementation: Is information provided on what will be the next steps for evaluation, validation and implementation?
- With regard to animal work
 - Has information been provided on husbandry and procedural refinements?
 - Has the number of animals been minimised?

Ethics and Research Governance of the proposal

- In completing this section 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?
- Where applicable, have replacement, refinement and reduction been applied to the proposed work?

Risks of research misuse

Please consider if there are any ethical, safety or security issues, or other potential adverse consequences, associated with the proposed research.

- 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?

Relevance to NC3Rs Strategy

Practical advances in applying the 3Rs to animal research are important in order to ensure high-quality, reproducible and humane science; and to address public concerns regarding the use of animals. One of the key aims of the NC3Rs is to promote the development of new research approaches, which have a reduced reliance on the use of animals and/or lead to improved animal welfare. The Centre does this partly through funding high quality research which advances knowledge in each of the 3Rs.

Please comment on the relevance of the proposal to the NC3Rs strategy.

- Is the relevance to the NC3Rs priorities clearly and convincingly explained?
- If this is a Strategic Award application, is the relevance to the call clearly explained?
- Have the applicants provided a clear assessment of the predicted advances in the 3Rs?
- Do you agree with this assessment?

4.5 Resources and Management

The NC3Rs abides by the RCUK policy regarding costs and uses the full economic costing (FEC) model for funding Project and Pilot Study grants and Strategic Awards. Reviewers are therefore not required to comment on the directly allocated or indirect costs of the application.

However reviewers should provide their views on direct costs of the proposal and the allocation of resources. Points to consider include:

- Is the number of staff appropriate for the work described, and are the justifications for consumables and equipment clearly set out?
- Is there sufficient justification for the resources requested?
- Have the applicants allocated time and proposed involvement in the research adequately?
- Is the use of animals justified in terms of need, species, number etc?
- Does the proposal offer value for money?

4.6 People

- Has the individual or group established a high quality track record in the relevant field? (N.B. this need not necessarily be in the field of 3Rs research, but in the investigator's own field)
- Where the proposal embarks on work in a field new to the applicants, or is a first funding application, is there a firm foundation to take the work forward with relevant expertise in place?
- How well does the work fit with other relevant research pursued by the applicants?
- What strategy do the applicants have in place to promote the proposed research to their scientific peers?

4.7 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. 0.5 integers 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
<p><u>Exceptional</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ 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 <p>3Rs Impact – Potentially very high e.g.:</p> <ul style="list-style-type: none"> ▪ Strategically important 3Rs area ▪ Replacing/reducing a large number of animals ▪ Refining a severe procedure (<i>even if numbers affected are low</i>) ▪ Applicable to other models ▪ Will have a local impact on animal use with a high likelihood of adoption by other groups nationally/internationally 	6
<p><u>Excellent</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ 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 <p>3Rs Impact – Potentially high e.g.:</p> <ul style="list-style-type: none"> ▪ Strategically important 3Rs area ▪ Replacing/reducing a significant number of animals ▪ Refining a severe/moderate procedure (<i>even if numbers affected are low</i>) ▪ 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 	5
<p><u>Very High Quality</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ 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 <p>3Rs Impact – Potentially medium/high e.g.:</p> <ul style="list-style-type: none"> ▪ Addresses an important 3Rs concern ▪ Replacing/reducing a significant number of animals ▪ Refining a moderate procedure (<i>even if numbers affected are low</i>) 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

<p><u>Good Quality</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ Worthwhile scientific question or knowledge gap ▪ Methodologically sound study ▪ Strong track record of the team and environment in this area ▪ Nationally competitive ▪ Ethical and/ or governance issues are well considered <p>3Rs Impact – Potentially medium e.g.:</p> <ul style="list-style-type: none"> ▪ Addresses an important 3Rs area ▪ Replacing/reducing a moderate number of animals ▪ Refining a moderate procedure (<i>even if numbers affected are low</i>) ▪ Could be applicable to other models ▪ Will have a local impact on animal use with potential for adoption by other groups 	3
<p><u>Fair Quality</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ 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 <p>3Rs Impact – Potentially low / medium e.g.:</p> <ul style="list-style-type: none"> ▪ 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
<p><u>Poor Quality</u></p> <p>Science</p> <ul style="list-style-type: none"> ▪ 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 <p>3Rs Impact – no (or very low) 3Rs impact e.g.:</p> <ul style="list-style-type: none"> ▪ 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
<p><u>Ineligible for funding</u></p> <p>(For Office use only NOT to be used by reviewer)</p>	0