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

NC3Rs Funding Schemes

Applicant and Grant Holder Handbook

Pioneering Better Science

Last updated October 2022

Contents

Introduction

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) is an independent scientific organisation. We lead the discovery and application of new technologies and approaches to minimise the use of animals in science and improve animal welfare (the 3Rs).

The NC3Rs was launched in 2004 and today we are the largest funder of 3Rs research in the UK and an authoritative international voice on the 3Rs.

The NC3Rs mission is to use the 3Rs principles to accelerate scientific discovery, support innovation and technological developments, and address societal concerns about animal research. One of the ways in which we further our mission is through our funding schemes, which provide opportunities for scientists at all career levels to engage with 3Rs research and training. Information on the following funding schemes can be found within this Handbook*:

- Project Grants
- Skills and Knowledge Transfer Grants
- Studentships
- Training Fellowships

The aim of this Handbook is to guide applicants through the funding process for these schemes. Additional help and information can be found on the NC3Rs www.nc3rs.org.uk.

If you need help completing the application forms in Je-S, please contact the Je-S helpdesk:

Email: JeSHelp@je-s.ukri.org

Phone: +44 (0) 1793 44 4164

For all other enquiries, contact the NC3Rs office:

Email: enquiries@nc3rs.org.uk

Phone: +44 (0)20 7611 2233

*Details of our open innovation scheme, CRACK IT Challenges can be found at https://nc3rs.org.uk/crackit/

1. The 3Rs

The principles of the 3Rs (**R**eplacement, **R**eduction and **R**efinement) were developed 60 years ago providing a framework for performing more humane animal research. Since then they have been embedded in national and international legislation and regulations on the use of animals in scientific procedures, as well as in the policies of organisations that fund or conduct animal research.

All submitted applications must be directed at one or more of the 3Rs (Replacement, Reduction and Refinement). When assessing applications, Panel members are asked to consider both the quality of the science and the likely 3Rs impact should the proposed research be successful. You are required to present a case for the potential 3Rs impact, with metrics, as part of your application.

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.

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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.

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.

2. NC3Rs Funding Scheme Remits and Eligibility Criteria

2.1 General overview

All of our schemes aim to encourage exceptional science and to have a measurable impact on the 3Rs. A summary of our funding schemes and the eligibility criteria is given in Table 1.

Overseas researchers may not be Primary Investigators but can be included as collaborators. In exceptional circumstances overseas researchers may be included as Co-Investigators, subject to prior discussion with the Office and where invited to do so; for example, where the nature of the research makes this necessary. Overseas Co-Investigator status is given at the discretion of the NC3Rs and approval must be sought before applying. **Any discussion with the NC3Rs regarding overseas Co-Investigator status and associated overseas costs should be noted in the cover letter of the Je-S application**.

Please note -

- Proposals relevant to any area of medical, biological or veterinary research or safety testing which support the development and application of the 3Rs will be considered.
- The same or similar application cannot be considered by any other Research Council, the Health Departments or any other research funder at the same time.
- Each Primary Investigator (PI) may submit a maximum of two applications per call deadline, with the exception of Fellowship applicants, who may only have one proposal under consideration by the NC3Rs at any one time. Applicants are advised to seek funding on the basis of the quality of their application rather than the number that can be submitted.
- If an NC3Rs grant holder has more than 12 months remaining on their NC3Rs grant, at the time of application, they are not permitted to apply as a Primary Investigator for further NC3Rs funding (excluding CRACK IT and Skills and Knowledge Transfer Grants – please contact the Office to discuss).
- Applications, including informal, formal and full applications, received after 4pm on the deadline date to any call will not be considered, without exception.
- PhD students cannot be requested as part of a non-Studentship grant as the NC3Rs has a separate Studentship Scheme for PhD projects.
- **Studentships** - Prospective students should note that the NC3Rs does not provide funding to students directly. If you are a student looking for funding for a studentship, please contact the relevant research institution.

Applicants are advised to read Section 5.5 and Section 5.7 of the MRC Guidance for Applicants should their proposal involve the development of software or induced pluripotent stem cells respectively.

Table 1: NC3Rs funding schemes and eligibility criteria

	Project Grants	Skills and Knowledge Transfer Grants
Scheme Description	▪ The NC3Rs Project Grant Scheme is our main funding scheme to support the development of new 3Rs approaches and technologies ▪ **Amount**: Dependent on the science ▪ **Duration:** Up to 36 months ▪ **Key dates:** Call opens in November; deadline in January; final decisions in July. ▪ This scheme is run annually. www.nc3rs.org.uk/funding/project-grants	▪ The NC3Rs Skills and Knowledge Transfer Scheme supports the adoption of alternative models, tools or technologies to drive 3Rs impact. ▪ **Amount:** Up to £75k (80% FEC) ▪ **Duration:** Up to 24 months ▪ **Key dates:** Call opens for informal outlines in November; full application deadline in February; final decisions in April ▪ This scheme is run annually www.nc3rs.org.uk/skills-and-knowledge-transfer-grants
Individual Eligibility*	▪ Applicants should be UK-based researcher(s) who can demonstrate that they will direct the proposed research and be actively engaged in carrying it through. ▪ The minimum formal qualification required is a graduate degree, although it would normally be expected that the applicant has been awarded a PhD. Applications involving less experienced researchers should be made in collaboration with more senior colleague(s). ▪ Applicants may already hold a grant from the NC3Rs and other funding bodies for research related to the topic for which new funds are being sought. It is important that applicants state whether any financial support from another body is already provided.	
Institutional Eligibility	▪ Higher Education Institutions (HEIs) ▪ Independent Research Organisations (IROs) ▪ Research Council (RC) Institutes	▪ Higher Education Institutions (HEIs) ▪ Independent Research Organisations (IROs) ▪ Research Council (RC) Institutes ▪ Small and medium-sized enterprises (SMEs)* Eligibility for joint awards may vary.
Start Dates	Successful applicants should expect to commence their projects between 1 August and 30 September of the year awarded.	Successful applicants should expect to commence their projects between 1 June and 1 August of the year awarded.

*The definition of small and medium-sized enterprises (SME) used by the NC3Rs is set out in the European Commission Recommendation of 6 May 2003. Please note that industry, including SMEs, are eligible to receive directly incurred costs only. Please see 4.2 (i) for further information.

	Studentships	Training Fellowship
Scheme Description	▪ The NC3Rs PhD Studentship Scheme aims to embed the 3Rs in the training of graduate scientists from a broad range of scientific backgrounds. ▪ **Amount:** Cash-limited award of £30k per annum ▪ **Duration:** 36 or 48 months ▪ **Key dates:** Call opens for informal outlines in April; full application deadline in July; decisions in October ▪ This scheme is run annually www.nc3rs.org.uk/funding/studentships	▪ The NC3Rs Training Fellowship Scheme aims to support the development of promising early career researchers with less than three years' post-doctoral experience, focusing on developing new skills and gaining a breadth of research experience. ▪ **Amount:** Applicants can apply for a commensurate salary (as agreed by the host research organisation) and up to £15k p.a. for other directly incurred research costs e.g. travel, consumables ▪ **Duration:** Up to 24 months ▪ **Key dates:** Call opens in July, full application deadline in September, decisions in December ▪ This scheme is run annually https://www.nc3rs.org.uk/training-fellowships
Individual Eligibility*	▪ A minimum of two Supervisors should be included on an application. Applicants should be UK researchers with a **minimum of five years postdoctoral experience.** ▪ The lead applicant must have a contract of employment with the RO that will outlast the duration of the proposed application. ▪ Researchers based in industrial and overseas organisations are not eligible to be Primary Investigators but they may be named as project partners or collaborators on applications. ▪ Applicants with limited supervisory experience should name more experienced colleagues as Co-Supervisors.	▪ This scheme is open to early career researchers **with a maximum of three years' postdoctoral experience** at the time of application. ▪ Final year PhD students may apply, but must be awarded their PhD before the Fellowship commences. ▪ Applicants with more than three years' postdoctoral experience who have had a career break or work outside of active research, should contact the Office to discuss their eligibility. ▪ Applicants are ineligible to apply if they already hold a permanent contract of employment at the host institution (e.g. lectureship position). **See additional requirements below.****
Institutional Eligibility	Eligible Je-S registered institutions and research organisations classified as follows: ▪ UK Higher Education Institutions (HEIs) ▪ Independent Research Organisations (IROs) ▪ Research Council (RC) Institutes The research organisation is responsible for recruiting students and for the administration of each Studentship award.	Eligible Je-S registered institutions and research organisations classified as follows: ▪ UK Higher Education Institutions (HEIs) ▪ Independent Research Organisations (IROs) ▪ Research Council (RC) Institutes Industrial organisations may act as collaborators but are not eligible to be primary host Research Organisations
Start Dates	Studentships must start by 1 October following award acceptance.	Fellowships can be activated as soon as an award has been finalised and must commence within 12 months of the award being made.

***Individual Eligibility Update**

If an NC3Rs grant holder has more than 12 months remaining on their NC3Rs grant, at the time of application, they are not permitted to apply, as a Primary Investigator, for further NC3Rs funding (excluding CRACK IT and Skills and Knowledge Transfer Grants – please contact the Office to discuss).

****Additional requirements for Training Fellowships**

- Applicants may have only one fellowship proposal under consideration by NC3Rs at any one time. However, they may simultaneously apply to other funders' Fellowship schemes.
- The applicant is responsible for finding a host Research Organisation who will act as their employer and will manage the administration of the Fellowship for the full duration of the award.
- There are no residency requirements and international applicants are eligible to apply. The onus is on the host Research Organisation to ensure all necessary work permits for the Fellow are in place.
- Each application must identify a sponsor at the host Research Organisation. If time will be spent outside the host Research Organisation, a Sponsor must also be identified at the collaborating institute. Industrial organisations may act as collaborating institutions but are ineligible to be primary host Research Organisations.
- Applicants may spend up to half of their award (12 months for Training Fellowships) at a second UK-based research organisation and up to six (6) months at an overseas or industrial partner's organisation. Applicants intending to spend longer periods abroad should contact the Office before submitting an application.
- Within their application, Training Fellowship applicants must also identify a Mentor at the host Research Organisation.
- It is expected that Fellowship holders will spend 100% of their time (based on a standard working week of 37.5 hrs) on the Fellowship. However, greater flexibility may be permitted during the second half of a fellowship and existing fellows wishing to dedicate over six hours a week to non-fellowship activities must contact the NC3Rs Office, prior to making any commitment, to request permission. Clinically qualified fellows (e.g. medical clinicians and veterinarians) can request to spend up to 20% of their time on clinical duties. In such cases, the NC3Rs will only meet the salary costs of the proportion of time spent on the Fellowship.

3. How to Apply

3.1 Outline application

Applicants are required to submit a proposal outline (including metrics on the potential 3Rs impact of the proposed research) **before** being invited to submit a full application. The purpose of this is to assess whether the proposals fall within NC3Rs remit and are suitable for the targeted scheme.

For all of our funding schemes, with the exception of Project grant and Training Fellowship applications, please complete the appropriate informal outline form and email it to the NC3Rs Office. Please see the relevant funding scheme web page for more information on outline submission deadlines.

Points to note:

- A formal outline submission, via the UKRI joint electronic submission system (Je-S), is required for **all Project grant** applications. Outline applications will be assessed by the Grant Assessment Panel. Only successful outline applications will be invited to submit a full application. Further information on completing the outline form for Project grant applications can be found in Section 4.1 Outline application – Project grants.
- At outline stage, **Studentship applicants** must provide the Office with (1) a completed outline form, (2) a letter of support from the Head of Department and (3) the main supervisor's CV (to include supervisory experience and not to exceed three sides of A4).
- **Training Fellowship applicants** are not required to submit an outline prior to submitting a full application but they are strongly encouraged to contact the Office to determine whether the proposed research fits the 3Rs remit and to confirm eligibility.

Please note that any outlines, both informal and formal, received after 4pm on the deadline date will not be considered, without exception.

3.2 Full application

All invited, full applications must be submitted via the UKRI joint electronic submission system (Je-S).

Please note for both formal outline and full applications - Once all the details of your application are complete you must submit it to your administering authority for approval; this is done via Je-S. This enables institutional checks to be carried out before final submission to the NC3Rs.

Please allow appropriate time **(a minimum of 5 working days)** before the submission deadline for this process as the final submission will come directly from the Research Organisation and must be made by the deadline or the application will not be accepted.

3.3 Guidance on using Je-S

Applicants must create an account in Je-S before they can access both the formal outline and full application forms. All user accounts will be automatically validated with the host organisation's research office. Applications cannot be submitted until the account is valid so please allow sufficient time for this process to be completed.

Submission of applications via Je-S

To access the application form you will first need to log-in to your Je-S account from the Je-S homepage and follow the instructions below:

1. Log in to the Je-S home screen.
2. Under 'Account', select 'Documents'
3. Then under 'Functions', select 'New Document'.
4. Then select Council (NC3Rs) and follow the prompts in Table 2 for the relevant funding scheme.

Table 2: Je-S prompts for NC3Rs funding schemes

Funding Scheme	Je-S Prompt		
	Document Type	**Scheme**	**Call**
Project Grants - Outline	Outline Proposal	Outline	Project Grant Outline
Project Grants - Full	Standard Proposal	Standard	Project Grant Full
Studentships	Studentship Proposal	Studentships	Studentship competition
Skills and Knowledge Transfer Grants	Standard Proposal	Standard	Skills and Knowledge Transfer
Training Fellowships	Fellowship Proposal	NC3Rs Fellowship	Training Fellowships

- Applicants should abide by the character limits indicated in each of the sections. Je-S will automatically truncate any words over the character limit. Microsoft Word should not be used for the character count as Je-S uses a different counting system to Word. Please use the character count feature within Je-S for this purpose.
- All fields in the form are mandatory and must be completed. Although Je-S may allow submission of the form if some sections are incomplete, your form will be returned upon receipt if it has been completed incorrectly. This will lead to delays in the processing of your application, including less time for the external peer review and PI response stages, if applicable.

3.4 Difficulties with Je-S

If you experience difficulties using Je-S or have questions regarding its use, contact the Je-S helpdesk:
Email: JeSHelp@je-s.ukri.org
Phone: +44 (0) 1793 44 4164

3.5 Resubmissions

- The NC3Rs does not allow resubmission of previously unsuccessful proposals, unless explicitly invited by the Panel. Proposals identified as uninvited resubmissions will not be processed.
- Where a resubmission is invited, a cover letter summarising the major revisions must accompany the proposal. Please note that our willingness to accept a revised proposal in no way implies that funding will be forthcoming.
- Proposals previously declined by the NC3Rs will not be considered by a Research Council within 12 months (from the date of submission) unless substantially revised. Please note this time restriction does not apply to outline applications.

- Our resubmissions policy is part of a suite of demand management measures, to help alleviate pressure on all involved with our peer review process.

The NC3Rs reserves the right to amend the application procedure.

4. The NC3Rs Application

All of our funding schemes require an application form and additional documents to be completed.

4.1 Outline Application - Project grants

Please note: This section applies only to Project grant applications and contains information on Je-S proposal form headings and attachments required for the formal outline. For information on the outline required for all other funding schemes please see section 3.

a. Project Details

Please select the Organisation you will be submitting the application from and the Department. If your Organisation is not listed you will need to contact your Research Office and ask them to register with Je-S. This process can take a number of weeks so please ensure that adequate time is allowed for registration to be completed. If the Organisation has provided you with a reference number, this can also be entered on this screen.

Please enter a submitters reference. This reference should be used to help distinguish between proposals in your current documents list and is unrelated to the reference that the organisation would be asked to provide if a grant were awarded.

Enter the title of the proposal (the title should be **non-confidential** as, if successful at the outline stage, it will be used when approaching candidate referees to review the full proposal).

Select the call you are submitting to from the drop-down list (e.g., Project grant).You must also enter the start date and duration of award for the grant (see Table 1 for further information).

b. Investigators

Please ensure all applicants are eligible to apply (see NC3Rs funding schemes and eligibility criteria**)** and that the inclusion of any overseas Co-Investigators has been approved by the NC3Rs Office. This approval must be mentioned in an accompanying cover letter.

More information on **Overseas Co-Investigator costs** can be found in the Resources section of the MRC Guidance for Applicants. The NC3Rs has adopted MRC policy.

Any collaborations with individuals or other departments within the same organisation as the Primary Investigator or any of the Co-Investigators should be noted in the Case for Support only.

c. Objectives

Please list the main aims and objectives of the proposal in order of priority.

d. Resource Summary

The following fields must be completed using Full Economic Costing (FEC). If nil costs apply, please insert a ‘0’ in the field. Although we do not require a detailed breakdown of costs at this time, the figures provided in the outline should represent the best estimates.

Directly incurred	These are costs that are explicitly identifiable as arising from the conduct of a project, are charged as the cash value actually spent and are supported by audit records. They include: staff, travel and subsistence, equipment and other costs, e.g. consumables
Directly allocated	These are costs of resources used by a project that are shared by other activities. They are charged to projects on the basis of estimates rather than actual costs and do not represent actual costs on a project-by-project basis. They include: investigators, estates and other costs (e.g. pool staff, IT systems)
Indirect costs	These are costs that are non-specific cost estimates charged across all projects that are not otherwise included as Directly allocated costs. They include the costs of the Research Organisation's administration such as personnel, finance, library and some departmental services.
Exceptions	These are Directly incurred costs that RC's will fund in full (e.g. at 100%), subject to actual expenditure incurred, or items that are outside FEC. Exceptional costs must be agreed with the Office in advance of submission, with approvals granted noted in an accompanying cover letter. At outline stage, these costings may include costs related to pieces of equipment costing more than £10k. The Research Organisation is expected to fund 50% of the FEC value for items of equipment over £10k and so only the amount requested from NC3Rs should be entered. Approval for equipment costs is **not** required but where exceptional costs relate to equipment please include this information within the cover letter.
Total cash contribution from Project Partners	These are cash contributions from the project partner to the project.
Total in-kind contribution from Project Partners	These are in-kind project partner contributions such as materials and equipment donated to the project, costs of any project partner staff to be seconded to the work, costs related to the use of facilities or equipment on the project partner's own premises, the costs to the collaborating body of providing staff time in project liaison, management and evaluation.

e. Summary

Please provide a scientific abstract in the "Summary" field. The summary should be **non-confidential** as, if successful at the outline stage, it will be used when approaching candidate referees to review the full proposal.

f. Project partners

Please enter the details of any Project partners. Please note; letters of support from Project partners are not required at this stage.

A Project partner provides a substantial intellectual contribution to the project, and their organisation may also provide resources either in-kind or financially. Project partners are not expected to request NC3Rs funding as part of the application.

g. Attachments – Outline application

Document type	Requirement	Page Limits	Je-S Attachment Type
Cover letter	optional	Up to 2 sides of A4	Proposal cover letter
Case for Support	compulsory	Up to 2 sides of A4	Case for Support
CVs	compulsory	Up to 2 sides of A4	CV

Case for Support: This document should contain a brief background of the scientific aims, a description of the experimental plan of the proposed project and include preliminary data.

The 3Rs objectives of your research **must** also be included in the case for support. You should explain **how** the proposed research will directly replace, reduce and/or refine the use of animals in research or testing (see Section 1 for definitions of the 3Rs) and provide supporting metrics. It is also important to outline your dissemination plan.

3Rs metrics can be estimated, for example, by searching literature databases to see how many papers are published each year reporting the use of the particular animal model and the typical number of animals used per experiment in the published papers. We recommend that you consider the following questions:

- Replacement/Reduction: How many animals would no longer be used per experiment/procedure/test? How many experiments/procedures/tests of this type are conducted in your laboratory? How many laboratories worldwide conduct these tests? What is the percentage reduction in animal use that could be achieved?

- Refinement: What is the evidence that animal suffering will be reduced/animal welfare improved? What objective indicators will be used to assess animal welfare? Is the severity limit for the procedure/protocol likely to be downgraded as a result of the proposed refinement technique? How many animals are likely to benefit per year both locally and in the wider scientific community?

CVs: Please provide CVs for the Primary Investigator (PIs) and Co-Investigators (Co-Is) only. CVs should not exceed 2 sides of A4 in length, including a list of the most relevant publications within the last five years. Please note that in line with MRC policy, the NC3Rs allows researchers to cite preprints in their grant applications. Preprints may be cited in applications only if they have a permanent identifier such as a DOI or any other persistent identifier and when they are less than five years old at the time the application is submitted.

The CV should only include information relevant to the application. Unnecessary personal data (eg home address, date of birth, personal phone numbers and emails) should **not** be included.

Please note – no additional attachments, e.g., Gantt charts, letters of support etc., are permitted at this stage. If, on addition of a project partner, Je-S requests a letter of support be uploaded, please upload a blank sheet only.

Cover letter: The inclusion of a cover letter is not compulsory but if the applicant wishes to supply one with their outline application they are welcome to do so. It may be added as an attachment on Je-S and should be no longer than two sides of A4. It must not be used to cover anything which should be included within the proposal form, Case for Support or other required attachments Any exceptions agreed with the Office such as Overseas Co-Investigators or exceptional costs should be included in this attachment.

4.2 Full Application – All funding schemes

A summary of the different requirements for each scheme's full application can be found in Table 3.

Guidance on completing the full application form for all funding schemes (with the exception of the Studentship Scheme) is given below.

Important points to note	
Studentship Scheme	▪ The Studentship Application form is different to those used for other schemes and so has a separate guidance which can be found under Section 4.4 Studentship Scheme Application Guidance. ▪ No period within the project duration should be solely used for writing the thesis. ▪ A 4-year PhD must not follow a 1+3 model and should be a stand-alone project for the duration.
Fellowship Scheme	In addition to the guidance provided in this section, guidance on completing additional headings required on the Training Fellowship application can be found in Section 4.3.
Skills and Knowledge Transfer Scheme	▪ The model/tool/technology, upon which the application is based, must be at a development stage appropriate for adoption by another laboratory. Some validation work to establish that the 3Rs approach is robust and reproducible in the end-user(s) lab, and/or to demonstrate that the 3Rs approach can be applied to a different research field or discipline is permitted. ▪ All applications to this scheme must include both the 'developer' and 'end-user(s)' of the model/tool/technology. Either party may be identified as the Primary Investigator, and the other(s) must be either named as Co-Investigator(s) or Project partner(s). ▪ Applicants are strongly advised to include a named researcher, who will be working on the award, within the staff details section of the Je-S form. ▪ Additional guidance on the application process and scheme remit can be found on the NC3Rs website.

a. Project details

Please select the Organisation and the Department you will be submitting the application from. If your Organisation is not listed you will need to contact your Research Office and ask them to register with Je-S. This process can take several weeks so please ensure that adequate time is allowed for registration to be completed. If the Organisation has provided you with a reference number, this can also be entered on this screen.

Enter the title of the proposal and select the call you are submitting to from the drop-down list (e.g., Project Grant). You must also enter the start date and duration of award for the grant.

Please enter a submitter's reference. This reference should be used to help distinguish between proposals in your current documents list and is unrelated to the reference that the organisation would be asked to provide if a grant were awarded.

Please note - Once all the details of your application are complete you must submit it to your administering authority for approval; this is done via Je-S. This enables institutional checks to be carried out before final submission to the NC3Rs.

Please allow appropriate time **(a minimum of 5 working days)** before the submission deadline for this process as the final submission will come directly from the Research Organisation and must be made by the deadline or the application will not be accepted.

b. Investigators

Please note - This section is not required for **Training Fellowship** applications.

Please ensure all applicants are eligible to apply (see NC3Rs funding schemes and eligibility criteria**)** and that the inclusion of any overseas Co-Investigators has been approved by the NC3Rs Office. This approval will need to be mentioned in the cover letter.

More information on **overseas Co-Investigator costs** can be found in the Resources section of the MRC Guidance for Applicants . The NC3Rs has adopted MRC policy.

Project partners should be named in the Case for Support, and a Letter of Support from each uploaded as an attachment. Any collaborations with individuals or other departments within the same organisation as the Primary Investigator, or any of the Co-Investigators, should be noted in the Case for Support only.

A Project partner provides a substantial intellectual contribution to the project, and their organisation may also provide resources either in-kind or financially. Project partners are not expected to request NC3Rs funding as part of the application.

Skills and Knowledge Transfer applications – It is advisable to include a named researcher who will be working on the award within the staff details section.

c. Objectives

Please list the main aims and objectives of the proposal in order of priority.

d. Summaries

The NC3Rs publishes the summaries from its grants on the NC3Rs website to demonstrate the potential impact of its funded research. Applicants are responsible for ensuring that any confidential information, or information that might be considered controversial or sensitive, is not included within the summaries.

In the "Summary" field, please describe the research in simple terms suitable for a lay audience.

In the "Technical Summary" field, please describe the proposed research in terms suitable for a specialist reader.

e. Academic beneficiaries

Please note - This section is not required for **Training Fellowship** applications.

Please describe who will benefit from your research. You should include details of academic or industry collaborators, areas of research the work could impact on, any clinical translation potential, as well as the general benefit to science.

f. Communications Plan

Please note - This section is not required for **Training Fellowship** applications.

The NC3Rs considers a strong communication and dissemination plan to be an essential factor in maximising the potential 3Rs outcomes of the grants and awards it makes. Please outline how you will communicate and disseminate your research to scientific audiences in order to promote uptake of its 3Rs benefits; this should not be limited to publications and conference attendance.

What plans, if any, do you have for communicating information about your work to the public? How are these plans supported by the host institution's own policies and facilities for communication with, and education of, the public?

g. Other support

Please list all the funding you have received in the past three years as either a Primary or Co-Investigator for work in a similar field of research to the current proposal. If you have submitted an application upon which you are still awaiting a decision, this will also need to be listed.

Please note - the same or similar grant application to the current proposal should not be submitted to another funding organisation at the same time.

The only exception to this is for the Training Fellowship Scheme, where applicants may simultaneously apply to other funders' Fellowship schemes but, they may only have one fellowship proposal under consideration by the NC3Rs at any one time.

h. Related proposal

Please note - This section applies only to **Project grant** and **Skills and Knowledge Transfer grant** applications.

If this application is a continuation of a previous NC3Rs grant or it is a resubmission, please provide details in this section.

Please see Section 3.5 for more information on resubmissions to the NC3Rs.

i. Financial information

The Resource Summary section will be automatically populated with the information you complete in the costings sections. In line with the Research Councils, applications should be submitted under the Full Economic Costing (FEC) model.

Please enter the costs being requested on the proposal under the relevant headings of Staff, Resources, Indirect and Estates costs. Costs should show 100% of the FEC. We will generally meet 80% of these costs (unless they are Exceptions).

Additional guidance on completing the **Resource section** can be found in the MRC Guidance for Applicants.

MRC University Units, MRC Units/Institutes and the Francis Crick Institute can apply for NC3Rs funding but applicants must follow the same costing guidance detailed in the MRC Guidance for Applicants, Section 3; Resourcing, when completing their application.

Applications from Industry

Industry organisations are not eligible for FEC funding and are only eligible to apply for funding from the NC3Rs as a Co-Investigator (with the exception of the Skills and knowledge transfer scheme to which SMEs are eligible to apply as lead applicant). Industry investigators are eligible for 100% directly incurred costs

only, which should be entered in the "Exceptions" section of the Je-S form with further explanation included in the justification of resources.

Please note: The information given here is not a substitute for taking legal or professional advice, which is the responsibility of the applicant. We cannot accept any liability for actions arising from the use of our guidance. The NC3Rs cannot be held responsible for the contents of any pages referenced by an external link.

Equipment Costs

- Single items of equipment costing less than £10k should be included in Other Directly Incurred costs, rather than under the Equipment heading. Items costing over £10k will require extra justification; evidence should be provided of an evaluation of the use of existing relevant equipment at the organisation and local collaborators.
- Further justification for all items of equipment costing between £10k (£8.33k ex VAT) and £138k (£115k excl. VAT) is required. The research organisation will need to provide extra justification for these items, providing evidence of an evaluation of the use of existing relevant capital assets.
- A business case, not to exceed more than two sides of A4, is required for all items of equipment above £138k (£115k excl. VAT) outlining the strategic need for the equipment (see UKRI website for further information).

Justification for resources requested must be provided as a separate attachment.
Any **exceptional costs** will need to be approved by the Office, in advance of submitting an application, with the details of this included in the cover letter.

Project grants	The financial support requested should be tailored by the scientific needs of the proposal and should be costed under the FEC model.
Skills and Knowledge Transfer grants	Grants are limited to a maximum of £75k (80% FEC value) of which a maximum of £30k may be requested as equipment costs. The UKRI policy on equipment costs applies to all funding requests made.
Training Fellowships	Funding for Training Fellowships is non-FEC and is paid directly to the host research organisation for the duration of the project (maximum of 24 months). Applicants can apply for a commensurate salary (as agreed by the host research organisation) and up to £15k per annum for other directly incurred research costs e.g. travel and consumables.

Points to note regarding Training Fellowship finances

- A brief breakdown of costs is required for audit and award purposes. Please enter the costs being requested on the proposal under the relevant headings of Staff and Resources. Indexation is not applied post-award.
- Indirect and Estates costs are not allowed under the terms of the Fellowship Scheme. Certain Directly Allocated costs are allowed but are restricted to the following headings: Animal costs, Costs for Research Facilities/Existing Equipment and Use of Research Council Facilities.
- The Salary costs for the applicant are captured in the "Fellow details" section and should not be re-entered in the Staff section. Once the Fellowship is awarded no additional requests can be made for supplementary salary costs. We would not normally expect to see other staff costs requested under this scheme, however there may be exceptional cases under which such costs would be justified, and these

costs should be listed here. All such requests must be discussed with and approved by the NC3Rs Office prior to submission.

j. Classifications

Under the “Board or Panel Portfolio” select all of the “Rs” your application will be addressing.

Complete the “Research setting” option to indicate the type of environment the work will be undertaken in. Clinically qualified candidates should also complete the questions relating to their clinical speciality and sub-speciality.

If the proposal uses human or biological samples, stem cells or will involve research in a developing country, please complete the relevant sections. If the proposal will develop technologies that can be used in a clinical setting, complete the “Technology Development” section.

Please include up to ten keywords in the “**Keyword**” section to highlight the scientific areas that will be covered in the proposal.

k. Ethical Information

Please complete all sections relating to ethical information around the use of human participants, animal research and genetic and biological risks.

Guidance on what to include in the “Animal Research”, “Animal Species” and other sections of the Application Form is given in Section 4.6: Use of Animals.

l. Reviewers

Please note - **This section applies only to Project grant full applications.**

Applicants have the option to nominate up to a **maximum of three** potential, national and international, reviewers for their application. A maximum of one of the three nominated reviewers will be contacted. Please note, that choices will be scrutinised by the Office for any conflicts of interest (including joint publications within the past five years) and it is not guaranteed that any suggested reviewers will be approached.

- Nominated reviewers must be experts in the research field and/or be able to provide an expert view on the value and benefits of the research proposal to users.
- Investigators shall not provide reviewers from their own organisation, or from current or proposed project co-funders, or where any possible conflict of interest may arise.
- If an applicant wishes to exclude potential reviewers from assessing their application, this should be noted in the cover letter, along with an explanation as to the reason for this exclusion. When detailing conflicted experts, the following information must be provided:
    1. The name of the person not to approach
    2. The RO(s) they are based at
    3. A clear reason why the person would not be able to provide an unbiased and evidence-based review
- The decision on whether or not to fulfil a request to exclude a reviewer lies with the NC3Rs following consideration of the justification provided. Requests submitted without a justification will not be considered.

Primary Investigator response to external peer reviewers' comments

Following external peer review, there is an opportunity for Primary Investigators to respond to peer reviewers' comments.

The response should be clearly presented and concise; with a minimum font size of 10pt Arial using an A4 format and **should not exceed three sides of A4**.

The response is to ALL reviews received. A subsequent response to any late reviews must also retain the response text on all earlier reviews and not exceed the specified page format. If the response needs to be amended (e.g. because of further later peer review comments), the existing copy will need to be removed and a new version uploaded.

4.3 Fellowship Scheme – Additional headings

Fellowship applicants are **strongly advised** to have their Sponsor(s) and/or Mentor review their application and provide guidance on the scientific content and grant writing process prior to submission. Confirmation that the application has undergone internal peer review must be included within the Sponsor's details section of the Je-S form or in a Letter of Support.

a. Fellow details

In the first **"Fellow"** screen, please enter the applicant name using the select option. Please complete the rest of the fields on the page.

You should also complete the salary details which should be agreed and approved by your Research Office and Head of Department. The salary of the Fellow should be set at a suitable spine-point by the Research Organisation and should be commensurate with experience. The NC3Rs reserves the right to reject a salary level it considers to be inappropriate. Once the Fellowship is awarded no additional requests can be made for supplementary salary costs. Indexation is not applied post-award.

b. Qualifications and experience

Applicants should detail their relevant experience to date including:

- Areas of research expertise
- Methods and techniques they have used
- Any prizes and awards won and details of any talks/presentations given (publications should not be included in this section)

Please note – the tick boxes on the Je-S form **must** be 'ticked' for the information to be included within the proposal. Omission of this information may result in rejection of the application.

c. Objectives

In the **"Objectives"** section please outline the main objectives of the proposed research in order of priority (not necessarily chronological).

d. Project partners

In this section please list any industrial or Project partners who will be providing support to the applicant in terms of cash or in-kind contributions.

- You will need to provide the full details of the organisation including the name of the contact and the type of contribution that will be made
- A fuller description of the input of the Project partner should be outlined in the Case for Support
- A letter of support from each named Project partner must also be included with the application

A Project partner provides a substantial intellectual contribution to the project, and their organisation may also provide resources either in-kind or financially. Project partners are not expected to request NC3Rs funding as part of the application.

e. Sponsor details

The Sponsor is the person who provides scientific guidance to the applicant. The aim of the Training Fellowships scheme is to allow the awarded Fellow to build an independent research career. As such the

research project should be distinct from that of the Sponsor; although it is recognised that often the science will be complementary to the work undertaken in the Sponsor's group.

The Sponsor should:

- State in what capacity they know the applicant
- Comment on the potential of the applicant to become an independent scientist
- Outline what guidance and support they will offer them including the research environment of the department and the facilities and expertise that will be available to the applicant
- Upload their CV - not to exceed three sides of A4 including relevant publications. The CV should only include information relevant to the application. Unnecessary personal data (eg home address, date of birth, personal phone numbers and emails) should **not** be included.

An applicant may identify more than one Sponsor if they feel additional expertise and guidance is needed; if so this section should be duplicated for each Sponsor. If significant time (three months or more) will be spent in a different organisation a Sponsor must also be identified at that organisation. The Sponsor's statement is an important consideration during the application's assessment.

f. Mentors

The Mentor is a person who provides guidance to the applicant, but is not directly involved in the research. It is a pastoral position, with the Mentor providing the Fellow with support, career guidance and an unbiased opinion. A letter of support from the Fellow's Mentor must be included as part of the application.

4.4 Studentship Scheme - Application guidance

This section of the handbook provides guidance on how to complete the Studentship Je-S application form and the NC3Rs Studentship Supporting Information form.

Guidance for completing the Case for Support, and all other attachments, is the same as for the other funding schemes and can be found in Section 4.5.

Studentship Je-S form headings

The Je-S form associated with this funding scheme does not capture all of the information required and so there is an additional form to complete. Please download the NC3Rs Studentship Scheme Supporting Information Form and complete in minimum Arial 10 pt font size.

On Je-S you will be asked to enter a submitter's reference. This reference should be used to help distinguish between proposals in your current documents list and is unrelated to the reference that the organisation would be asked to provide if a grant were awarded.

a. Research Organisation

Please select the Organisation and department from which you will be submitting the application. If your Organisation is not listed you will need to contact your Research Office and ask them to register with Je-S. This process can take a number of weeks so please ensure that adequate time is allowed for its completion before the submission deadline.

b. Contact details - Grant Holder

The name and organisation details of the Primary Supervisor of the PhD student need to be entered on this screen. Please ensure the primary applicant is eligible to apply, further information can be found in Section 2 NC3Rs Funding Scheme Remits and Eligibility Criteria.

c. Project summary

This section should include a summary of both the project's scientific and 3Rs aims.

A statement summarising **how** the proposed research will replace, reduce and/or refine the use of animals in research or testing (see Section 1 for definitions of the 3Rs) **must** be included. As part of this statement, it is important to describe how the proposed work will impact the 3Rs locally (i.e. within your own laboratory) and more widely (nationally/internationally). The statement should also include **metrics** of the potential 3Rs impact (e.g. scale of reduction in the numbers of animals used) and describe how a robust 3Rs legacy will be generated.

The NC3Rs publishes the abstracts from its funded grants on the NC3Rs website. Please ensure that this summary is suitable for web publication if an award is made.

This summary should be the same as that provided under 'Project Summary' on the Supporting Information Form.

NC3Rs Studentship Scheme Supporting Information Form

This form must be attached using the "**Other Attachment"** attachment type. Although Je-S may allow applicants to submit the application without this form, applications received without this document will not be considered.

Please follow the guidance below in order to ensure that the form is completed according to NC3Rs requirements.

a. Research proposal

Within this section, please add the following information:

a) The project title
b) A list of the main objectives of the proposal which should include consideration of how to establish a 3Rs legacy
c) A project summary, summarising both the scientific and 3Rs aims of the project and suitable for publication. This should be the same summary as provided on the Je-S form.
d) Select which 'R' the studentship proposal addresses
e) Indicate if the proposal is a resubmission

b. Supervisor details

Please provide the contact details of all Supervisors. Each application must have a minimum of two Supervisors with each Supervisor having a **minimum of five years postdoctoral experience** at the time of application. Less experienced Co-Supervisors will be considered on a case-by-case basis.

Each Supervisor is required to upload a CV (of no more than three sides of A4 in length) as part of the application. CVs should detail the Supervisor's relevant research and supervisory experience, including submission rates and publications. The CV should only include information relevant to the application. Unnecessary personal data (eg home address, date of birth, personal phone numbers and emails) should **not** be included.

Please note – a letter of support from the Head of Department must also be uploaded as part of the application.

Adding a new supervisor on the supporting information form

Double click the 'Add New Supervisor' macro. This will prompt a pop-up window to appear. Click 'yes' to add the additional supervisor section. Please note, this will create a copy of the section and its contents in its entirety, so applicants should add all additional sections required prior to adding content.

c. Training, Monitoring and Research Environment

Within a) please describe the training and support that will be provided for the student at the Research Organisation (RO). Summarise the key features of (i) generic and transferrable skills training, in line with the "Researcher Development Statement" developed by Vitae, and (ii) the mentoring and professional guidance, to be provided over the course of the studentship. Training and support over and above standard policies should be included.

It is important to describe how the proposed Studentship will meet the NC3Rs objectives and to detail the specific 3Rs training and courses that will be provided for the student in b).

The 3Rs training should aim to develop a solid understanding of what the 3Rs are and how to implement them in practice, as well as provide 3Rs relevant learning, networking and/or dissemination opportunities for students. Training should go beyond legal requirements and should be tailored to each proposal.

Possible 3Rs training activities include:

- Engagement with the NC3Rs through online resources, attendance at relevant meetings and intreactions with Regional Programme Managers
- Encourage discussion of the 3Rs by convening meetings
- Meetings with relevant RO staff (i.e., NACWO)
- Observe 3Rs relevant RO meetings
- Create a 3Rs culture within lab groups/ departments

A proposal can include an element of multidisciplinary research training at a Project partner organisation. Please provide details of the contribution and training that will be provided by the Project partner and describe how it will benefit the student's research and training within c).

Where a student will receive training at multiple locations and/or in multiple disciplines, applicants should explain how they will ensure that the student's training remains coherent and achievable, and also include a robust mitigation plan within their application.

Within d), describe the type of environment in which the student will work, i.e. quality of environment, surrounding scientific and 3Rs expertise, the student experience, the learning potential and supervisory arrangements etc. Also describe whether there are any special facilities or features available that would enhance the student's training and skills development.

The methods of feedback and assessment that will be provided to the student during their studentship should be summarised in e).

d. Funding Breakdown

All NC3Rs Studentship awards are made as cash limited awards of £30k per annum, for either three or four years, that are paid directly to the Research Organisation over the course of the award. Although justification for costs and a detailed breakdown are not required, funds do need to be allocated into one of three fund headings, as listed below:

i. **Student Stipend** – Set by the host institute and must meet the minimum level set out by UKRI. This amount may be increased, at your discretion, using the funds provided by the NC3Rs, if you believe it will allow you to recruit the most suitable candidate.

ii. **Fees** – Set by the host institution at which the degree will be registered.

iii. **Research Training Support Grant (RTSG)** – All remaining funds should be allocated into this heading; the RTSG is intended for use in paying for expenses which the student's Supervisor/ department deem to be in direct support of a student's research, such as, but not limited to:

- Laboratory consumables
- UK and international conferences and summer schools (including the NC3Rs Studentship events and meetings)
- UK fieldwork expenses
- Language training courses, usually undertaken in the UK prior to an overseas fieldwork trip
- Reimbursement of interpreters, guides and assistants
- Survey costs (e.g. printing, stationary, telephone calls etc.)
- Purchase of small items of equipment (e.g. cameras, tape recorders, films, cassettes or telephone and photocopying facilities in the department/faculty)

e. Ethical Information

Please provide details, including justification, if you are using animals as part of the Studentship proposal. If you are using cats, dogs, equidae and/or non-human primates, please complete the appropriate section in Annex 1 of the form. Further guidance on justifying the use of animals is given in Section 4.6 of this Handbook. This section is mandatory for all applications.

f. Data Preservation for Sharing

The NC3Rs expects valuable data arising from NC3Rs-funded research to be made available to the scientific community with as few restrictions as possible. For this reason, you must include a data sharing and preservation strategy statement following, where appropriate, the MRC's policy and data access principles (MRC Data Sharing Policy).

4.5 Attachments – all funding schemes

The "Attachments" section of the form should be used to upload specific documents that are required as part of your application.

Please select the type of document you are attaching by selecting the appropriate descriptor from the drop down list under the "Document type" tab. The table below illustrates attachments that should be provided for each scheme.

Please note - You may only attach PDF, postscript or Microsoft Word files – all documents can be drafted offline and will be converted to PDF files once uploaded. Please take care when naming attachments as these will be seen by the Panel. Please ensure files are given a logical file name and description so they can easily be found.

Additional considerations

- If you wish to include letters of support/collaboration, quotes for equipment, or extra details on ethical issues, please upload these as separate attachments in the "Attachments" section in the Je-S application form.

- Applications cannot be supplemented with further information after the deadline for submissions has passed. As such, please ensure that all information and attachments, as per the scheme requirements, are uploaded as part of the application at the time of submission.

Table 3: Breakdown of documents required by funding scheme

	Project Grant (Outline)	Project Grant (Full)	Studentship	Training Fellowship	Skills and Knowledge Transfer grant
Je-S Application Form	✓	✓	✓	✓	✓
Case for Support	✓	✓	✓	✓	✓
Justification of Resources	✗	✓	✗	✓	✓
Data Management Plan (DMP)	✗	✓	✗	✓	✓
Letters of Support	✗	Optional	HoD letter compulsory*	HoD letter compulsory*	Optional
Supporting Information Form	✗	✗	✓	✗	✗
CVs**	✓	✓	✓	✓	✓
Personal Statement	✗	✗	✗	✓	✗
Cover Letter	Optional	Optional	Optional	Optional	Optional
Experimental design appendix OR EDA report	✗	✓	✓	✓	✓

*HoD – Head of Department
** Fellow and Sponsor CVs should be uploaded as part of all Fellowship applications

a. Writing a Case for Support

The Case for Support should include more detailed information on the scientific proposal, potential 3Rs outputs and outcomes, past achievements, environment, people involved in the proposed work and references.

The guidelines below list general considerations to be taken into account when writing the Case for Support. Each proposal is unique, and it is each applicant's responsibility to ensure that all relevant information is provided.

Before writing the Case for Support, applicants are advised to refer to Section 5: NC3Rs Assessment Procedures, where links to guidance provided to peer reviewers and the Panel can be found.

The maximum length of the Case for Support for each funding scheme is listed in Table 4. The length stated is inclusive of any references, figures and figure legends. The Case for Support should be submitted via Je-S as a PDF attachment and can be drafted offline.

Table 4: Maximum length of the Case for Support by funding scheme

Funding Scheme	Maximum Length
Project grant – outline application	Up to 2 sides of A4
Project grant – full application	Up to 9 sides of A4
Skills and Knowledge Transfer grant	Up to 5 sides of A4
Studentship	Up to 5 sides of A4
Training Fellowship	Up to 5 sides of A4

Format and length

The Case for Support should be written in a minimum of Arial 10 pt font size, with margins of 2cm at the left, and 1.5cm on all other borders.

Please note - Justification of resources should not be included within the Case for Support. This information should instead be supplied in a separate attachment, see sub-section (i) for further information.

Content

Before beginning, please be clear as to which area of the 3Rs your proposal contributes. Evaluation of proposals will take into consideration both the quality of the science and the likely 3Rs impact should the proposed research be successful. Therefore, the overall score of an application will combine the scientific and 3Rs evaluation of the proposed research. Please visit the NC3Rs website for more information.

Scientific importance and potential 3Rs outcomes

Please highlight:

1) **Which** of the 'Rs' applies to the proposed research
2) **How** the replacement, refinement and/or reduction would be achieved
3) The likely **scale** of replacement/reduction in animal use and/or improvement in animal welfare, both locally (i.e. within your own laboratory) and in the wider research community (nationally/internationally)
4) The ways in which the 3Rs outputs of the research will be promoted to the wider scientific community to encourage and drive **uptake**. This should include robust plans for a 3Rs legacy and

acknowledge the expectation of publishing methodologies on the NC3Rs Gateway, or on another freely accessible platform.

It is particularly important to provide **metrics** around the potential 3Rs impact. Estimates can be made, for example, by searching literature databases to see how many papers are published each year reporting use of the particular animal model and the typical number of animals used per experiment in the published papers.

We recommend that you consider the following questions:

- **Replacement/Reduction:** How many animals would no longer be used per experiment/procedure/test? How many experiments procedures/tests of this type are conducted in your laboratory/company? How many laboratories/companies worldwide conduct these tests? What is the percentage reduction in animal use that could be achieved?

  Example: If successful, the new assay will use 1 rat/experiment when 30 rats are currently needed using the standard method. This represents 97% reduction in animal use/experiment.

- **Refinement**: What is the evidence that animal suffering will be reduced/animal welfare improved? What objective indicators will be used to assess animal welfare? Is the severity limit for the procedure/protocol likely to be downgraded as a result of the proposed refinement technique? How many animals are likely to benefit per year both locally and in the wider scientific community (nationally/internationally).

All applicants must also demonstrate how they will build and sustain a 3Rs legacy, as maximum 3Rs impact can only be achieved if an approach is adopted by others. It is essential to build in a clear and reasonable dissemination plan and give sufficient detail regarding how adoption by others will be achieved beyond the lifetime of the award.

For more information on 3Rs metrics, please refer to the NC3Rs Evaluation Framework.

Research plans

Give details of the experimental approaches, study designs, and techniques that will be used. It is not necessary to describe each experiment, but enough detail must be provided to show how and why the research is likely to be competitive in its field and that it has been carefully planned to provide useful and reliable results.

- Explain the need for research in this area and how, if successful, it will benefit medical, veterinary or biological research. In some instances, it is useful to include letters of support from the research community as a measure of this need. If the work has potential application to other research areas, it also may be beneficial to describe this.

- Highlight plans that are particularly original or unique.

- Explain in greater detail how new techniques, or particularly difficult or risky studies, will be tackled and describe plans for alternative approaches should these fail. The inclusion of a Gantt chart is encouraged.

- Give sufficient details of other past and current research to show that the aims are scientifically justified, and to show that the proposed model/technique will add distinct value to the one currently used or in development by others.

- Identify facilities or resources you will need access to.

- If the sex of the animals, humans, tissues or cells to be used in the study cannot be stated in the experimental design and methodology appendix, a justification for this must be included in the case for support.

- For animal experiments, provide as much detail as possible. See Section 4.6 of this Handbook for further guidance.

- It is expected that both sexes will be included in animal experiments but if a single-sex study is proposed, applicants must justify why using both sexes is not appropriate or possible. More information on the use of both sexes in experimental design can be found on the NC3Rs website and the Experimental Design Assistant.

- Include details about animal care, housing and husbandry, refinements to procedures, and any welfare assessments that will be carried out.

- If successful, what will be the next steps for evaluation, validation and implementation? How will this be achieved? What, if any, additional steps will be required before an advance in the 3Rs can be implemented?
  If these plans have been discussed with an industrial partner, it is important to include this and provide details. Letters of support from industrial collaborators can be included as part of the application.

- Is the proposed research likely to generate commercially exploitable results? What arrangements and experience does the research group or the host institution have to take forward the commercial exploitation of research in this area? Any plans must be realistic and credible and if discussed, please include the appropriate industrial links.

For **Skills and Knowledge Transfer grants:**

- Applicants should justify their choice of model/tool/technology, provide a brief description of similar models already available and outline both the scientific and 3Rs advantage(s) of their chosen model/tool/technology over the alternatives described.

- Call specific guidance on completing the case for support can be found on our scheme webpage.

- The research plans for Skills and Knowledge Transfer grant applications must outline well-defined milestones, at quarterly intervals, and also include a Gantt chart as part of the case for support.

Environment, people and track record

Describe how the scientific environment in which the research will be done will increase the chances of success. Does your proposal include suitable expertise? Are all appropriate areas covered?

- Explain how the research will benefit from facilities provided by the host institution.

- Describe any collaboration needed to support the research, or to help translate it into practice. Please include letters of support.

- The Je-S application form will ask for details of other research funding held to be included. Describe the research support (aims, value, staff) available which is relevant to the NC3Rs proposal.

Please note - preliminary data and GANTT charts must be included in the Case for Support and not as separate attachments.

b. Experimental design and methodology appendix or EDA Experimental Design report

All applicants are required to include an experimental design and methodology appendix or an EDA Experimental Design report, to provide additional information on the proposal's experimental design and methodology.

Experimental design and methodology appendix

This appendix is solely for the provision of information relating to the experimental design and methodology of the proposed research and must not be used as a continuation of the Case for Support. Applicants should not duplicate information presented elsewhere in the application, particularly when already provided within

the Je-S proposal form and the Case for Support. All applications are checked by the NC3Rs Office. Those where the Experimental design and methodology appendix is deemed to be incomplete will be returned.

The appendix must not exceed **one side of A4** in length and should be clearly labelled as the 'Experimental design and methodology appendix' at the end of the main case for support. Where appropriate, the use of figures, tables and/or diagrams is encouraged. Applicants are encouraged to seek input from those with the relevant statistical and/or methodological expertise to review their proposed experimental design and analysis plan.

In many instances this section may include statistical power calculations based on justifiable and explicit assumptions about the anticipated size and variability of the experimental effects. If statistical power calculations are not given, applicants should provide a principled explanation of the choice of numbers.

Power calculations can be used to calculate the minimum sample size required so that it is reasonably likely to detect an effect of a given size, or to calculate the minimum effect size that is likely to be detected in a study using a given sample size. Explanations based solely in terms of 'usual practice' will be considered insufficient. An overview of the planned statistical analyses and their relation to the choice of sample size should be included.

What to include in the appendix

Robust methodology and experimental design should be at the centre of any proposal to aid reproducibility of research findings. Below is a summary of key points taken into consideration during the peer review of applications.

If your proposal includes the use of animals, please note this summary is not exhaustive and should be used in conjunction with the information provided in Section 4.6: Use of Animals.

In the appendix, applicants are required to clearly describe and justify the following:

- State the sex of the animals, humans, tissues or cells to be used in the study. If the sex cannot be stated, provide a justification for this in the case for support.
- Measures for avoidance of bias, for example masking (also known as blinding), randomisation, inclusion and exclusion criteria.
- Number of experimental and control groups and sample size per group, along with a clear definition of the experimental unit.
- How the sample size was calculated, showing power calculations and including justification for the effect size chosen.
- For circumstances in which power calculations are not appropriate, justify why a power calculation is not appropriate and provide a principled explanation of the choice of numbers.
- Description of the planned statistical analysis methods that will be used, explaining how they relate to the experimental design and showing that they are appropriate for the types of data that will be collected.
- Frequency of measurements/interventions to be used.

Where the proposal includes the use of animals, please refer to the **NC3Rs Experimental Design Assistant (EDA)** (https://eda.nc3rs.org.uk) for guidance on experimental design and sample size calculation.

Applications that do not provide sufficient detail to convince peer reviewers and Funding Panels that the proposed experiments will be carried out appropriately to produce robust and reproducible research will be rejected for funding on these grounds and subject to the usual limits on resubmission.

The NC3Rs Experimental Design Assistant (EDA) and Experimental Design report

Where the proposal includes the use of animals, applicants are encouraged to use the EDA (https://eda.nc3rs.org.uk) to design experiments. The EDA captures methodological details about the experimental plan in the form of a diagram, and provides tailored guidance and feedback on the design. It can then generate a PDF report which provides a transparent description of the experimental design in a standardised format. Applicants are encouraged to upload the EDA Report in place of the 'Experimental design and methodology appendix' to their case for support.

c. Letters of Support

Letters of support may be included in full applications to all of our funding schemes and may come from a number of sources including collaborators, industrial partners etc.

The letter must:

- Be dated, signed and on headed paper.
- Should confirm the role the collaborator/industrial partner will have in the research including details of any expertise or resources that will be provided.

Applications to our **Studentship and Fellowship schemes** must include a letter of support from the Head of Department at the host Research Organisation.

Head of Department letters should state that the host Research Organisation will 1) administer the award for the duration, 2) guarantee that the Fellow/ PhD student will have access to space and facilities to carry out the project and 3) detail the types of ongoing activities within the department that support 3Rs training.

The letter may also comment on how the applicant will fit into the department and their scientific potential, as well as outlining the research environment of the department and the facilities, expertise and support that will be available to the applicant.

d. Data Management Plan (DMP)

The NC3Rs has adopted the MRC policy on data management and research data sharing. All applications (excluding Studentship applications) are required to upload a Data Management Plan (DMP) as an 'Additional Document' attachment type as part of the application on Je-S. The DMP should comply with the MRC's Policy on Research Data Sharing. The DMP should demonstrate how the applicant will meet, or already meets their responsibilities for research data quality, sharing and security. It should refer to any institutional and study data policies, systems and procedures and be regularly reviewed throughout the research cycle. The DMP is reviewed by peer reviewers alongside the Case for Support. The data management plan template can be used to develop a DMP to accompany a research proposal. If it is not used, then the applicant should ensure that all the topics listed on the template are addressed. The length of the DMP will be dependent on the complexity of the data collected, but should be between **half a page to a maximum of 3 pages**.

e. CVs (PIs and Co-Is)

All applicants (Primary and Co-Investigators, Fellows, Sponsor(s) and Supervisor(s)) should upload a *curriculum vitae* (CV) in the **"**Attachments**"** section.

CVs added on Je-S should not exceed **three sides of A4** in length (minimum Arial 10pt font size) and should detail employment history, qualifications, funding history and a selection of relevant publications.

Please note –

- The CV should only include information relevant to the application. Unnecessary personal data (eg home address, date of birth, personal phone numbers and emails) should **not** be included.

- CVs submitted by Studentship Supervisors should include the Supervisor's relevant research and supervisory experience; including submission rates and publications.
- CVs should clearly show why the group is best placed to successfully undertake this research. However, if it is not obvious, you may wish to elaborate further in the Case for Support.
- The NC3Rs allows researchers to cite preprints in their Grant, Fellowship and Studentship applications. Preprints may be cited in applications only if they have a permanent identifier such as a DOI or any other persistent identifier and when they are less than five years old at the time the application is submitted.

f. Personal Statement

This attachment is only required for applicants to the **Training Fellowship Scheme.** Applicants should upload their personal statement as an 'Additional Document' attachment type with their application on Je-S.

In no more than **one side of A4,** applicants should summarise why they are the best candidate for an NC3Rs Training Fellowship, outlining their future career ambitions and how they will use this award to access skills' training and career development support that will underpin their future career. Applicants should use this statement to highlight relevant experience and/or characteristics that have not already been illustrated within other sections of the application. For more guidance on the types of skills and competencies that potential applicants should seek to demonstrate, please refer to the NC3Rs Skills and Experience Framework.

g. Cover Letter

The inclusion of a cover letter is not compulsory but if the applicant wishes to supply one with their application they are welcome to do so. It may be added as an attachment on Je-S and should be no longer than **two sides of A4**. It must not be used to cover anything which should be included within the proposal form, Case for Support or other required attachments

Any exceptions agreed with the Office such as overseas Co-Investigators or exceptional costs should be included in this attachment, as well as the names of any conflicted experts that you request not to be used as reviewers (where applicable). For conflicted experts, please include the name and RO of the person to be excluded and the reason why they should not be approached.

Please note - cover letters will not be sent to peer reviewers and will only be made available to the NC3Rs and Panel members. Any confidential or other information you do not wish the peer reviewers to see should therefore be included within the cover letter.

h. Justification of Resources (JoR)

Research Council guidance on writing a good Justification of Resources (JoR) document is available on the Je-S Help Pages. The role of the JoR is to aid reviewers when assessing proposals so that they can make an informed judgement on whether the resources requested are appropriate for the research posed.

For more information on completing the Justification of Resources document please see the MRC Guidance for Applicants.

Guidance on **Full Economic Costing and Special Considerations** can also be found in this Handbook.

The JoR should be **no more than two sides of A4,** and is a free text document, which is uploaded as an attachment to the proposal. This statement should be used to justify the resources required to undertake the research project and is required for all applications (excluding Studentship applications). The JoR should explain why the resources requested are appropriate for the research proposed, taking into account the nature and complexity of the research proposal. It should not be simply a list of the resources required as this is already given in the Je-S form. All items requested in the Je-S form must be justified in the JoR.

4.6 Use of Animals

The elaboration of a compelling scientific case is an essential prerequisite for justifying the use of animals. Over the past few years there have been a number of important initiatives that have been aimed at raising the sometimes inadequate standard of reporting of animal experiments in the scientific literature. The NC3Rs ARRIVE guidelines, for example, lay out criteria that should be met when reporting animal studies in order that their results and conclusions can be properly evaluated by readers. These criteria address a range of issues relating to transparency and validity of experimental design, the avoidance or minimisation of bias and the adequacy of the statistical aspects of the study including statistical power and appropriate statistical analysis.

In light of these initiatives, the NC3Rs and other UK research funders have revised and updated their guidelines on what information needs to be provided to allow proper evaluation of the scientific strengths and weaknesses of applications for funding involving animal use. In some cases, adherence to the principles in this Section will require additional resources, e.g. for 'chipping' animals or increased maintenance charges resulting from the randomisation procedure, or salary costs associated with obtaining statistical support. The NC3Rs recognises this and such costs should be fully justified in the appropriate sections.

General points

Applicants are expected to have developed their proposals in accordance with the cross funder guidance for the use of animals in research Responsibility in the Use of Animals in Bioscience Research and, in the case of use of non-human primates, the NC3Rs Guidelines: Primate Accommodation, Care and Use.

Experiments using animals funded by the NC3Rs must comply with the Animals (Scientific Procedures) Act 1986, amended 2012 (ASPA) and any further embodiments, in:

- using the simplest possible, or least sentient, species of animal appropriate
- ensuring that pain and distress are avoided wherever possible
- employing an appropriate design and using the minimum number of animals consistent with ensuring that scientific objectives will be met

Advice on opportunities and techniques for implementing these 3Rs principles can be found on the NC3Rs website.

Researchers using animals are strongly advised to read this section carefully before preparing a proposal to ensure all the relevant information required is included in the appropriate sections of their application. In particular, applicants should ensure their proposal clearly sets out and justifies the following:

- research objectives and how the knowledge generated will advance the field
- the need to use animals and the lack of realistic alternatives
- choice of species of animals to be used
- sex of the animals to be used in the study and if a single-sex study is proposed, justify in the case for support why using both sexes is not appropriate or possible
- type of animal(s), for example, strain, pathogen free, genetically modified or mutant

Experimental design, avoidance of bias and statistical considerations

There are a wide range of designs and approaches to animal experimentation that are appropriate depending on the objectives of the research proposal. In all cases, the NC3Rs expects that researchers provide well justified information in their applications concerning the experimental design and its suitability to answering the research questions posed. Applicants should therefore provide adequate justification for their choice of design and numbers of animals and interventions. Where animals are used in multiple types of experimental approach within a single application (e.g. for tissue supply, pilot experiments or more defined pre-clinical studies), exemplars for these types of experiment should be provided. It is important that adequate information is also given concerning methodological issues including (but not restricted to) the bullet points below.

1. Objectives and experimental outcomes

- Primary and any secondary objectives of the study, or specific hypotheses being tested
- Primary and secondary experimental outcomes to be assessed (e.g. cell death, molecular markers, behavioural changes)

2. Experimental approach

- Relevant information about the animals to be used (e.g. species, strain, sex, developmental stage, weight)
- Number of experimental and control groups
- Steps taken to minimise the effect of bias, for example masking/blinding, randomisation, inclusion and exclusion criteria.
- How randomisation will be carried out (if used) or why it is not appropriate; how the sex of animals will be taken into account in the allocation of animals to experimental groups.
- How blinding/masking will be implemented or why it is not appropriate.
- The number of different time points at which measurements will be made on each animal, number of interventions to be used.

3. Sample size

- Total number of animals to be used in each experiment.
- Definition of the experimental unit and the implications thereof (that is there is a difference between N samples from one animal, as distinct from one sample from each of N animals/or combining samples from multiple animals).
- How the sample size was calculated, showing power calculations and including the primary outcome measure the calculation is based on and justification for the effect size chosen.
- For circumstances in which power calculations are not appropriate, justify why and provide a principled explanation of the choice of numbers.

4. Planned statistical analyses

- Description of the planned statistical analysis methods that will be used, explaining how they relate to the experimental design, how they take the sex of animals into account and showing that they are appropriate for the types of data that will be collected.
- Details of any statistical advice sought/available

Please refer to the **NC3Rs Experimental Design Assistant (EDA)** (https://eda.nc3rs.org.uk) for guidance on experimental design and sample size calculation.

Where to provide the information

Guidance on where in the proposal each of the aspects should be addressed is given below and summarised in Table 6.

This information must be provided for all proposals involving animals (including where the only procedure is Schedule 1 killing), regardless of whether or not the animal costs are requested as part of the proposal. Applicants should note that these sections, although not part of the main Case for Support, will be subject to equally careful scrutiny, and will carry substantial weight when assessing the scientific strength of the proposal.

a. Je-S section on ‘Animal Research’

Under the “Animal Research” section please state whether the proposal will involve the use of vertebrate animals or other organisms covered by the ASPA and Directive 2010/63/EU. Please provide details of any procedures categorised as moderate or severe in accordance with the maximum prospective severity rating in the Home Office licence under which the work will be carried out, how the procedure is undertaken,

adverse effects experienced by the animals, and measures taken to minimise any pain, suffering, distress or lasting harm.

b. Je-S section on 'Animal Species'

This section must be completed for all proposals involving animal use, irrespective of whether funding for the animals is requested as part of the proposal. Select ALL the species that will be used for the research. Select 'Supporting Information' to enter your justification for animal usage.

If use of **non-human primates, cats, dogs, pigs or equines** will be involved in the project, further information will be required. All applications which involve the use of these higher species are reviewed by the NC3Rs Office to ensure the usage is fully justified and that the welfare and husbandry standards are optimal. The additional information provided in this section is used for this purpose; therefore it is imperative that all of the questions are fully addressed.

Under '**Supporting Information'** please provide:

- Sound scientific reasons for the use of animals and an explanation of why there are no realistic non-animal alternatives
- An explanation of how the choice of species complies with the Animals (Scientific procedures) Act (1986). For knockout or transgenic lines this should include information on the sources these may be obtained from and relevant information to demonstrate the verification of lines selected.
- An explanation of how and why the animal species and model being used can address the scientific objectives and the relevance to human biology.

Applicants are encouraged to provide other 'supporting information' regarding experimental design, statistical analyses etc. in the 'Experimental design and methodology' appendix to the case for support or an EDA Experimental Design report and not in the Je-S application form.

c. Je-S section on 'Resources – Animal costs'

The costs of both the animals themselves and their maintenance may be requested and should be listed in the 'Resources – Animal Costs' section of the Je-S form. Please see the relevant Je-S Help page for more information.

Animal costs may be shown as either Directly Incurred or Directly Allocated costs. Please state if the weekly maintenance costs are an actual (Directly Incurred) or an estimated (Directly Allocated) cost.

Where experiments involve genetically altered animals, examples of the breeding strategies should be included in the Justification of Resources attachment to support the total number of animals requested. The focus of this attachment should be to justify the resources requested for breeding, maintaining and using the chosen number of animals; the scientific and statistical justification of how the chosen number of animals was arrived at must be included in the 'Experimental design and methodology' appendix to the Case for Support or an EDA Experimental Design report. Please refer to the NC3Rs Breeding and Colony Management resource for guidance on breeding and colony management strategies.

Applicants contemplating the use of animals purchased from commercial suppliers should, wherever possible, use UK suppliers, to minimise the risk of suffering during transport. For cats, dogs and primates, Home Office-approved suppliers must be used. Applicants planning research using rhesus macaques should obtain animals from the Centre for Macaques.

d. Proposal attachment 'Justification of Resources'

A detailed justification of the costs incurred should be given in the Justification of Resources attachment (see section 2.2 of MRC Guidance for Applicants for further information). This should detail the animal costs requested, and may outline breeding programmes if appropriate to support the number of animals required. No experimental or statistical details should be included in this section; these details must be included in the 'Animal Species' section of the Je-S form and Case for Support.

e. Proposal attachment ‘Case for Support - Experimental design and methodology appendix or EDA Experimental Design report’

The experimental plans should be detailed in the one page appendix to the Case for Support entitled ‘Experimental design and methodology appendix’ or an EDA Experimental Design report.

The experimental design should be outlined, including a justification of the total numbers of animals to be used and, where appropriate, the frequency of measurements/interventions required on each animal. Planned procedures to minimise experimental bias (for example, randomisation protocols, blinding) should be outlined or an explanation included as to why such procedures are not appropriate. Each experiment does not need to be described in detail, but sufficient information must be included that reviewers are readily able to understand the experimental plan.

Researchers must provide a properly constructed justification of how the numbers of animals to be used were determined. In general it would be expected that professional statistical advice will be sought in putting this section together.

In many instances this section will include statistical power calculations[3] based on justifiable and explicit assumptions about the anticipated size of the experimental effects. If statistical power calculations are not given, applicants should provide a principled explanation of the choice of numbers. In general, explanations based solely in terms of ‘usual practice’ will not be considered adequate. An overview of the planned statistical analyses and their relation to the choice of sample size should be included.

It is essential that the case is clearly made as to how the chosen design (with reference to the information regarding the numbers of animals and planned statistical analyses provided) will enable the stated objectives of the study to be achieved. In addition to the usual background and specification of the primary and secondary objectives of the study, or specific hypotheses being tested, the primary and secondary experimental outcomes to be assessed should be clearly defined (e.g. cell death, molecular markers, behavioural changes). Each experiment does not need to be described in detail, but sufficient information must be included that reviewers are readily able to understand the design rationale and make robust judgements on the scientific case.

[3] Power calculations can be used to calculate the minimum sample size required so that one can be reasonably likely to detect an effect of a given size, or to calculate the minimum effect size that is likely to be detected in a study using a given sample size.

Use of animals overseas

If your project involves the use of animals overseas you must upload to Je-S a signed Letter of Support from both the UK and overseas applicants stating that:

- They will adhere to all relevant national and local regulatory systems in the UK and overseas.
- They will follow the guidelines laid out in the Responsibility in the Use of Animals in Bioscience Research and ensure that work is carried out to UK standards.
- Before initiation of the proposed research work, appropriate approvals from Institutional and/or central animal ethics committees will be obtained for experimental protocols to be adopted in their projects. Successful proposals may be expected to provide copies of these permissions before funding is released.
- Details on where the animal research will take place (UK or overseas) and through which funder the resources are being sought.

If the research involves the use of rodents, rabbits, sheep, goats or pigs overseas, please also complete the appropriate 'Additional Questions' form, and upload as a letter of support, as part of your application, to Je-S.

Additional guidance on conducting and reporting animal research can be found on our Peer review and advice service hub.

Ethical and welfare standards and review

Applicants must ensure that best practice in relation to animal husbandry and welfare is followed. Where the work proposed is not covered by an existing Project Licence under the ASPA, applicants should put their proposals to the local Animal Welfare and Ethical Review Body (AWERB) for review prior to submission and ensure that all of the ethical and welfare issues raised are addressed.

If applicants are proposing to undertake any animal experiments as part of collaborative programmes outside of the UK, these experiments must be conducted in a way that conforms to the legislation in that country. In addition, ethical and welfare standards equivalent to those provided in the UK (e.g. under the ASPA) must be applied and maintained (see p14 of Responsibility in the Use of Animals in Bioscience Research).

Advice on choosing appropriate contractors, especially for preclinical studies, is given in this PDF presentation.

Home Office licences

It is the responsibility of all applicants to ensure that the appropriate Home Office licences are obtained. This will include the requirement that the research proposals are approved by the local AWERB.

Home Office licences (or amendments to existing licences) do not have to be obtained before the application is submitted to the NC3Rs, but if a grant is awarded, researchers must have the necessary licences in place before any animal experimentation begins.

Mouse strains

The NC3Rs encourages the archiving and sharing of genetically altered mouse strains as a means of both reducing and refining animal use[4]. The MRC supports a central repository of mouse strains, the Mouse Frozen Embryo and Sperm Archive (FESA) at MRC Harwell. FESA aims to ensure that valuable mouse strains are safeguarded, that the need to maintain colonies of live mice for long periods of time is reduced, and that the significant investment in engineering strains is capitalised upon fully.

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[4] See "https://www.nc3rs.org.uk/3rs-resources/breeding-and-colony-management/sharing-and-archiving-ga-mice".

Where there may be a need for the repeated creation of pre-existing genetically modified mouse strains, this must be fully justified. Applicants planning to produce genetically modified mouse strain(s) should investigate whether suitable strains are available via FESA or elsewhere before requesting resources for creating new strains. Applicants planning on creating new genetically altered mouse strains as part of their work should actively consider archiving and sharing these strains via FESA. When archiving and sharing of genetically modified mice is not possible, please clearly state in your application the reasons for this.

Contact: FESA
Email: fesa@har.mrc.ac.uk

Table 6: Justification of animal use checklist

Where a proposal involves multiple experiments (e.g., pilot study, tissue supply, treatment comparison) the level of detail shown below should be included for each type of experiment.

Information required in attachments

'Experimental design and methodology' appendix or EDA Experimental Design report	**1. Objectives and experimental outcomes** ▪ Primary and any secondary objectives of the study, or specific hypotheses being tested ▪ Primary and secondary experimental outcomes to be assessed (e.g. cell death, molecular markers, behavioural changes) **2. Experimental approach** Relevant information about the animals to be used (e.g. species, strain, sex, developmental stage, weight) ▪ Number of experimental and control groups ▪ Steps taken to minimise the effect of bias, for example masking/blinding, randomisation, inclusion and exclusion criteria. ▪ How randomisation will be carried out (if used) or why it is not appropriate; how the sex of animals will be taken into account in the allocation of animals to experimental groups. ▪ How blinding/masking will be implemented or why it is not appropriate. ▪ The number of different time points at which measurements will be made on each animal, number of interventions to be used. **3. Sample size** ▪ Total number of animals to be used in each experiment. ▪ Definition of the experimental unit and the implications thereof (that is there is a difference between N samples from one animal, as distinct from one sample from each of N animals/or combining samples from multiple animals). ▪ How the sample size was calculated, showing power calculations and including the primary outcome measure the calculation is based on and justification for the effect size chosen. ▪ For circumstances in which power calculations are not appropriate, justify why and provide a principled explanation of the choice of numbers. **4. Planned statistical analyses** ▪ Description of the planned statistical analysis methods that will be used, explaining how they relate to the experimental design, how they take the sex of animals into account and showing that they are appropriate for the types of data that will be collected. ▪ Details of any statistical advice sought/available
Justification of Resources attachment*	**Explanation of funding requested** Details required: ▪ Overview of how the figure for funding requested was reached - no experimental or statistical details should be included here ▪ A breeding plan for rodents may be included to justify the total number of animals requested

* For Studentship applications, please use the Animal Research section of the Studentship Supporting Information

Information required within the Je-S form

Animal Research section of the Je-S form*	**Procedure severity** Details required: ▪ Confirmation of the use of animals – tick Yes even if animal costs are not being requested ▪ Details of any procedures categorised as moderate or severe under ASPA
Animal Species section of the Je-S form under 'Supporting Information' for each species*	**The need to use animals and the choice of species** Details required: ▪ Sound scientific reason for the use of animals ▪ Explanation of why there are no realistic non-animal alternatives ▪ Explanation of how the choice of species complies with ASPA **Justification of the choice of species/ model:** Details required: ▪ Explanation of how and why the animal species and model being used can address the scientific objectives and the relevance to human biology
Animal Costs section of the Je-S form*	**Funding requested** Details required: Total number of animals requested: ▪ List of the associated purchase and upkeep costs

* For Studentship applications, please use the Animal Research section of the Studentship Supporting Information

5. Assessment Procedures

All applications are checked by the NC3Rs Office. Those that do not fit the remit will be returned and not assessed by the Panel.

For further information on the assessment procedures for each scheme, please see the relevant page listed below.

- Project Grants: Assessment Procedures and Grant Assessment Panel
- Skills and Knowledge Transfer Grants: Assessment Procedures and Skills and Knowledge Transfer Assessment Panel
- Studentships: Assessment Procedures and Studentship Assessment Panel
- Training Fellowships: Assessment Procedures and Training Assessment Panel

On these pages you will find the following information:
Considerations for the informal outline stage (where applicable)
Assessment and Scoring Criteria for referees (where applicable)
Assessment and Scoring Criteria for Panel members (outline and full application stages, where applicable)
Panel membership
Declarations of Interest

Please note that funding decisions are final and are not open to appeal.

All applicants will receive their decision letter after the Panel meeting. Estimated dates of when applicants can expect to be informed of funding decisions can be found in Table 7.

The NC3Rs reserves the right to amend the application process.

Table 7: Panel outcome notification

Funding Scheme	Informed of Outcome
Project Grants	Post-outline application stage: Mid-March Post-full application stage: End of July
Skills and Knowledge Transfer Grants	End of April
Studentships	End of October
Training Fellowship	Mid-December

6. Confidentiality and what information will be made available to others

The NC3Rs is committed to its mission of using 3Rs principles to accelerate scientific discovery, support innovation and technological developments, and address societal concerns about animal research. The NC3Rs will handle all applications for funding in confidence, however applicants should note that in certain circumstances it will be necessary to share the information submitted with different audiences. The guidance below provides more information on this.

a. Peer review

The NC3Rs has adopted the MRC's Peer Review Process. These webpages explain:

- How the Peer Review process is used by the NC3Rs to make funding decisions.
- What information will be made available to peer reviewers as part of the decision making process and what information will be made available to applicants about the assessment of their proposal.
- What information is routinely published relating to Peer Review and the funding of proposals.
- The approach taken by the NC3Rs in responding to requests for information that is not routinely published.

b. Declarations of interest – Panel members:

NC3Rs Panel members are required to comply with the UKRI Conflicts of Interest Policy. Members are required to declare any private, professional or commercial interests that might, or that might be perceived to, conflict with the NC3Rs' interests.

Interests for members of the research panels are declared under the following categories:

- Personal remuneration (employment, pensions, consultancies, directorships, honoraria etc.)
- Registrable shareholdings and financial interests in companies
- Research income
- Major academic collaborations (national and international)
- Unremunerated involvement with and membership of bioscience, bio-medical, pharmaceutical/chemicals industry, healthcare provision or science policy/communication and similar activities/organisations
- Political/pressure group associations

Declarations of interest for current NC3Rs Funding Assessment Panels can be found on the web pages listed in Section 5: Assessment Procedures.

c. What we publish on our website

Details of information that is routinely published on awarded grants can be found in the Peer Review Framework, however it should be noted that there are some differences for NC3Rs grants.

The information that the NC3Rs will publish on their website include the following:

- Grant holder names, including co-applicants
- Host institution and location
- Value and duration of award
- Research project title
- Lay summary

- Scientific summary
- Project summary
- 3Rs and research classification
- Potential 3Rs impact
- Keywords
- Grant associated publications and other outcomes

d. Freedom of Information Act (FOIA)

The FOIA gives anyone the right to request access to information held by the NC3Rs, including the information relating to applications and the peer review process.

The NC3Rs is an independent, scientific organisation and has responsibility for setting its scientific strategy and making funding decisions. However, it is not an independent public authority. The NC3Rs utilises some MRC systems and processes and for the purposes of the Freedom of Information Act (FOIA) is considered as part of the MRC, which in turn is part of UK Research and Innovation (UKRI).

Any request for information will be considered on a case by case basis and the NC3Rs will work with the MRC/ UKRI to ensure that the information is handled appropriately and that any sensitive material is correctly identified and has the relevant exemptions of the Act applied. The NC3Rs and the MRC/UKRI will seek the views of the applicant and the research organisation wherever possible, and will consider these opinions in their deliberations. Further information on the approach taken can be found in the MRC Policy on Peer Review.

7. Our Expectations for NC3Rs Grant Holders

In this section, applicants and existing Grant holders can find information concerning the NC3Rs expectations of its Grant holders.

For the 3Rs impacts of a project to be fully realised, NC3Rs-funded work needs to be widely disseminated and adopted by the scientific community. We aim to support our Grant holders in these activities as much as possible, and we will arrange meetings to discuss a grant during the lifetime of the award.

Information on Post Award processes (including grant extensions, requests for suspensions and transfers) can be found on our website and in the MRC Guidance for Applicants.

a. Terms and conditions

All NC3Rs Grant holders must:

- Implement the principles in the cross council guidance Responsibility in the Use of Animals in Bioscience Research.
- Where non-human primates are used, implement the principles in the NC3R Guidelines: Primate Accommodation, Care and Use
- Abide by the Animal welfare standards expected of suppliers of antibodies when purchasing custom-made antibodies and peptides.
- Aid the NC3Rs in its peer review process**,** as a condition of the grant and under reasonable circumstances, by providing a referee report if requested.

Holders of NC3Rs research grants (**Project Grants, Skills and Knowledge Transfer Grants and Training Fellowships**) are expected to abide by the UKRI Terms and Conditions and additionally to the NC3Rs-specific Terms and Conditions. Any additional NC3Rs conditions will be included in the award letter.

Grant holders will be invited to a number of NC3Rs events during the term of their award. Where attendance is compulsory, this will be indicated in the event invitation. For **Studentships,** the main Supervisor and student must attend. This will assist us in our strategic aim to forge links between researchers and improve dissemination of the research we fund.

It is a condition of NC3Rs Training Fellowships that **Fellows** must attend an annual Fellows Meeting. Similarly, it is a condition of NC3Rs Studentships that PhD **students** attend NC3Rs Studentship events and meetings.

Studentship Holders must abide by the Terms and Conditions of UKRI Training Grants along with expectations of the Research Councils on skills training requirements for research students.

b. Publications and Open Access Publishing

The NC3Rs has adopted the UKRI's policy on open access of publications, with the overall aim of disseminating publicly funded research to the widest possible community; not only to promote the scientific outputs, but also to ensure the highest level of utilisation and awareness of 3Rs methods. Holders of NC3Rs research grants are expected to disseminate their results by publishing in appropriate scientific journals, detailing the 3Rs impact of the work.

Grant holders must ensure that all outcomes of NC3Rs-funded research including the data, results, final conclusions and any other information relating to the research are published on a freely accessible platform in accordance with the UKRI policy on Open Access. All grant holders must ensure that the methodologies developed as part of NC3Rs-funded project(s) are published on the NC3Rs gateway or on another freely accessible platform.

Peer reviewed papers reporting research that is wholly or partially funded by the NC3Rs must:

- Be published in journals which are compliant with the UKRI policy on open access.

- Include details of the funding that supported the research - NC3Rs support for an individual or research project must be acknowledged on all publications where such support has been significant (i.e. accounts for at least 20% of funding).
- Provide a statement on how the underlying research materials such as data, samples or models can be accessed.
- Make reference to the 3Rs implications of the research, including in the abstract and the main body of the text. It is a missed opportunity if publications from NC3Rs-funded grants are published without the 3Rs impacts being articulated.
- In addition, researchers should ensure that they report animal-based studies in accordance with the ARRIVE guidelines as far as possible, taking into account the specific editorial policies of the journal concerned.
- The NC3Rs should be informed of any publications or other promotional material or events arising from the grant; please email a PDF copy to the appropriate mailbox.

From 1 April 2013 and until further notice, UKRI will solely pay for Article Processing Charges (APCs through block grants to UK Higher Education Institutions, approved independent research organisations and Research Council Institutes. Grant applications will no longer include provision for open access publication or other publication charges. Applicants should not include any costings for APCs or other types of publication in respect of peer reviewed research articles and conference proceedings that acknowledge funding from the NC3Rs.

The NC3Rs contribution to APCs is paid via the MRC contribution to the UKRI block grant. To encourage adoption of the open access policy, the NC3Rs has joined Europe PubMed Central (Europe PMC).

All grant holders must deposit any publications arising from NC3Rs funded-research into **EuropePMC** at the time of final publication, as defined in Annex 1 of the UKRI Open access policy.

c. Reporting requirements and evaluation

Information on the outcomes of NC3Rs research funding is vital to our evaluation activities and helps us to make the case for continued substantial public investment in 3Rs research.

The NC3Rs uses Researchfish (www.researchfish.com)) for the collection of NC3Rs grant outputs and outcomes data and for monitoring the progress on grants both during and after the lifetime of the award. You will receive log-in details from Researchfish Ltd. and will then be able to check, add to and edit your outputs and outcomes data.

Grant holders must use Researchfish to report on their grant periodically and when requested to do so by the NC3Rs or Researchfish. You can input data into Researchfish all year round, and are asked to formally submit your information during an annual submission period. There is also a requirement to update Researchfish when your grant is coming to an end. Failure to update Researchfish within three months of the grant end date will result in an automatic financial penalty.

Table 8: Our reporting requirements

Who?	▪ Compliance with Researchfish reporting is a requirement for every grant issued by the NC3Rs (including CRACK IT awards) ▪ The PI is responsible for their Researchfish submission, but can give access to other team members to help input information
When?	▪ Grant holders can, and should, submit information to Researchfish all year round and **for at least five years** after the grant has ended ▪ In line with the Research Councils, the NC3Rs also has an **annual collection period** ▪ There is also a requirement to update Researchfish **when your grant is coming to an end**
What?	▪ 3Rs question set - detailing the 3Rs impacts of the grant ▪ Details of all outputs, outcomes and impacts, when available, arising from the grant ▪ We have published an Evaluation Framework for assessing 3Rs impact. The Framework provides examples of the types of metrics that Grant holders should report in Researchfish
Why?	▪ To showcase your impacts and achievements ▪ To identify how we can use our expertise and networks to help maximise your impacts - both scientific and 3Rs ▪ To monitor progress on grants. Researchers who do not report into Researchfish when requested to do so, or use the system inappropriately, may be **subject to sanctions** (withholding or claw-back of grant payments) and will become ineligible to apply for additional grants from the NC3Rs (and potentially the Research Councils). A flag will be applied on the grant's system so that all Research Councils are aware of the failure to report ▪ Researchfish is not a publicly accessible data repository. However, data held in Researchfish may be used by the NC3Rs to populate our website and for production of publications such as our Annual Report and Research Review

Changes to an NC3Rs-funded project

Grant holders must inform and consult with the NC3Rs if there are any significant changes that may affect the progress or delivery of the project and its potential to realise a 3Rs impact. No substantive changes to the experimental design of a project involving the use of animals, which might affect the ethical characteristics of the award, are allowed without the prior approval of the NC3Rs.

If a Grant holder proposes to make significant changes to their NC3Rs-funded project, the NC3Rs reserves the right to request revised proposals for its approval. Where significant changes are proposed, the NC3Rs may decide to make a new grant in place of the existing grant, or to revise, retain or terminate the existing grant.

Mid-award progress report and meeting(s)

In addition to the reporting requirements on Researchfish, Grant holders are required to complete a mid-award progress report template. Grant holders will be contacted in advance to schedule a meeting to discuss the progress report form. Members of the NC3Rs team and, in some cases an NC3Rs Board member, will attend on behalf of the NC3Rs. Where applicable, NC3Rs students must also attend.

The NC3Rs reserves the right to sanction, and in exceptional cases to terminate, a grant at any stage if unsatisfactory progress has been made.

Queries about our reporting requirements should be sent to 3Rsgrants@nc3rs.org.uk

Appendix – Useful links

Websites and Email Addresses

1. NC3Rs website: www.nc3rs.org.uk
2. Project grants and Skills and Knowledge Transfer grants: 3Rsgrants@nc3rs.org.uk
3. Studentships: studentships@nc3rs.org.uk
4. Fellowships: fellowships@nc3rs.org.uk
5. NC3Rs Office: enquiries@nc3rs.org.uk
6. Animals (Scientific Procedures) Act 1986
7. The Principles of Humane Experimental Technique

Funding Scheme Web pages

1. Project Grants
2. Skills and Knowledge Transfer Grants
3. Studentships
4. Training Fellowships

Je-S

1. Je-S Homepage: Je-S Login
2. Je-S helptext
3. Je-S email address: jeshelp@je-s.ukri.org

Funding scheme informal outline form

1. NC3Rs Informal Outline Form - Studentships
2. NC3Rs Informal Outline Form – Skills and Knowledge Transfer

Guidance and policies

1. NC3Rs Evaluation Framework
2. NC3Rs Skills and Experience Framework
3. MRC – Equipment Guidance
4. MRC Data Sharing Policy
5. MRC Guidance on Data Management Plan
6. Data Management Plan Template
7. Additional questions on the use of rodents overseas
8. Peer review and advice service hub
9. NC3Rs Breeding and Colony Management resource

MRC Guidance for Applicants

1. MRC Guidance for Applicants

Studentships Application and Studentship Grant Holders

1. Studentship Supporting Information Form
2. Annex 1 (Use of non-human primates, cats, dogs or equidae)
3. UKRI Doctoral Stipend Levels and Indicative Fees
4. 'Researcher Development Statement' developed by Vitae
5. UKRI Guidelines - Studentships
6. UKRI Training Grants Terms and Conditions

Confidentiality

1. MRC's Peer Review Process
2. UKRI Conflicts of Interest Policy

Existing NC3Rs Grant Holders

1. Information for Existing Grant Holders
2. UKRI Terms and Conditions
3. NC3Rs Specific Terms and Conditions
4. UKRI Training Grants Terms and Conditions
5. Animal welfare standards expected of suppliers of antibodies
6. ARRIVE Guidelines
7. Responsibility in the Use of Animals in Bioscience Research
8. NC3Rs Guidelines: Primate accommodation, care and use
9. UKRI Policy on Open Access
10. Europe PubMed Central

Reporting and Evaluation

1. Researchfish – www.researchfish.com
2. Our reports and reviews

NC3Rs,
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London,
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020 7611 2233
www.nc3rs.org.uk