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

NC3Rs Project grants scheme

Applicant guidance for submitting a full application

Pioneering Better Science

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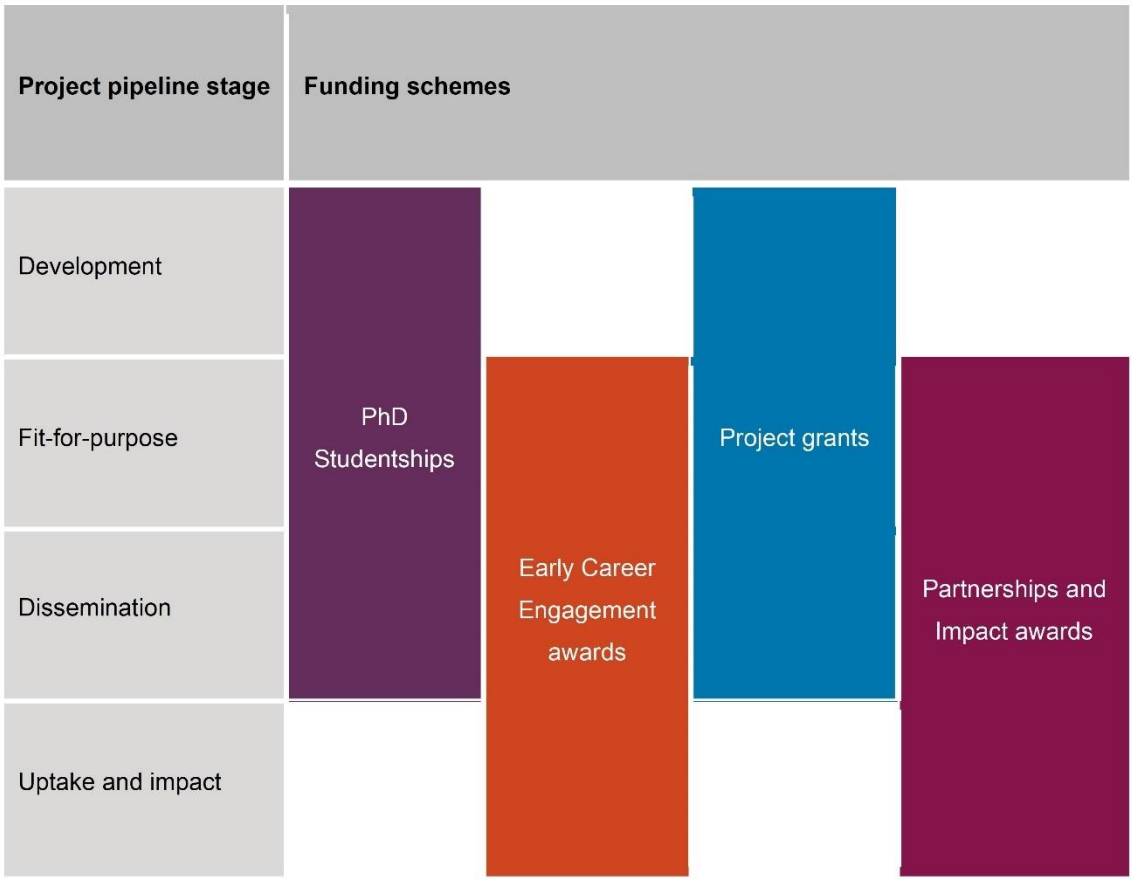
Contents

1. Overview

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) funds multidisciplinary research to provide 3Rs models, tools and technologies that scientists in academia and industry can use to answer important questions to generate new knowledge, improve human and animal health and protect the environment.

Through our funding schemes our goal is to provide 3Rs models, tools and technologies that are well-characterised and ready for deployment, and importantly are better than existing approaches in terms of their predictivity, reliability, reproducibility, cost and impact on animal welfare. Our funding schemes provide opportunities for scientists at all career stages to engage with 3Rs research and training, and support the initial development of 3Rs approaches, their characterisation to demonstrate that they are fit-for purpose and sharing across the wider community to encourage uptake and their use into routine practice. We refer to this as our project pipeline – there are four steps in the pipeline which are detailed below. Our funding schemes map across the pipeline as shown in Figure 1. Detailed definitions of each stage of the project pipeline and supporting examples can be found in the Appendix.

Figure 1: NC3Rs Funding schemes mapped onto the project pipeline



This document provides guidance to prospective applicants applying to the Project grant scheme. The Project grant scheme supports the first three steps of the project pipeline (as shown in Figure 1) – the development of 3Rs approaches, their characterisation to demonstrate that they are fit-for purpose and dissemination

activities to promote awareness within the wider scientific community. An application to the Project grant scheme must be focused on at least two of these three steps of the project pipeline.

1.1 The 3Rs

The principles of the 3Rs (**R**eplacement, **R**eduction and **R**efinement) were developed over 50 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 focus on advancing the 3Rs. Panel members are asked to assess both the quality of the science and the likely 3Rs impact should the proposed research be successful.

There is some variation in the exact interpretation of the 3Rs. The NC3Rs has updated the definitions in line with common scientific parlance to highlight the importance of the 3Rs to modern research practices.

Table 1: Definitions of the 3Rs

3Rs	Basic	Updated
Replacement	Avoiding or replacing the use of animals in areas where they otherwise would have been used.	Accelerating the development and use of predictive and robust models and tools, based on the latest science and technologies, to address important scientific questions without the use of animals.
Reduction	Minimising the number of animals used consistent with scientific aims.	Appropriately designed and analysed animal experiments that are robust and reproducible, and truly add to the knowledge base.
Refinement	Minimising the pain, suffering, distress or lasting harm that research animals might experience.	Advancing research animal welfare by exploiting the latest *in vivo* technologies and by improving understanding of the impact of welfare on scientific outcomes.

1.2 Scheme overview and remit

The NC3Rs Project grant scheme aims to support the development of new 3Rs approaches and technologies.

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

Table 2: Overview of the Project grant scheme

Scheme at a glance

▪ The NC3Rs Project grant scheme aims to support the development of new 3Rs approaches and technologies.
▪ Applications may be for up to 36 months in duration.
▪ The amount requested should be dependent on the science. Awards are funded at 80% of the full economic cost (FEC).
▪ Project grant funding competitions are run annually. Key dates include:
  ▪ Informal outline deadline – January
  ▪ Full application deadline – April
  ▪ Applicants informed of outcome – July
  ▪ Awards must start by 1 October following award acceptance
▪ The NC3Rs does not permit resubmissions, please see section 2.1.2 for more information.

Individual eligibility
▪ Applicants should be UK-based researchers who can demonstrate that they will direct the proposed research and be actively engaged in accomplishing the project's aims. ▪ 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). ▪ 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 Project Lead for further NC3Rs funding (excluding CRACK IT and Partnerships and Impact awards – please contact the Office to discuss). ▪ Researchers based in overseas organisations and/or in industry are not eligible to apply as Project leads (please see sections 3.2.1 and 3.2.2, respectively, for further guidance).
Establishment eligibility

▪ Any UK research establishment can apply, including:
  ▪ Higher Education Institutes (HEIs).
  ▪ Independent Research Organisations (IROs).
  ▪ Research Council (RC) Institutes.

2. The application process

2.1 How to apply

2.1.1 Formal outline application

Applicants are required to submit a formal outline of the research proposal through the UKRI Funding Service.

Outline applications are assessed by the Grant Assessment Panel. Only successful outline applications will be invited to submit a full proposal.

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 Project lead may submit a **maximum of two** applications per call deadline. Applicants are advised to seek funding on the basis of the quality of their application rather than the number that can be submitted.

2.1.2 Full application

All invited, full applications must be submitted through the UKRI Funding Service.

Please note for both formal and full applications: Once all the details of your application are complete you must submit it to your research office for approval; this is done via the Funding Service. This enables institutional checks to be carried out before final submission to the NC3Rs.

Please allow appropriate time (a minimum of **five working days**) before the submission deadline for this process as late applications will not be accepted, without exception. The research office is responsible for submitting the completed and checked application.

2.1.3 Using the Funding Service (TFS)

For assistance with using the Funding Service, please contact support@funding-service.ukri.org or call the UKRI Funding Service Helpline: +44 (0)1793 547 490.

2.1.4 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 to the proposal must be submitted to the NC3Rs Office by email. 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 in the assessment process.

The NC3Rs reserves the right to amend the application procedure.

3. The full application

This section contains guidance on how to complete the full application form on the UKRI Funding Service. Sub-sections are named as they appear in the application form.

Please note that limited attachments are permitted.

To start an application on the Funding Service use Opportunity reference: **OPP530: NC3Rs Project grants 2024 – Full application stage**.

It is strongly recommended that the person who starts and completes the formal outline application is the Project Lead.

3.1 Application details

Please note: the Application name and Summary should be **non-confidential** as, if successful at outline stage, they will be used when approaching candidate referees to review the full proposal.

- **Application name** – Enter the name of the formal outline application. The title of the project should also be relevant to the 3Rs.
- **Summary** – Please provide a scientific abstract in the Summary field. The limit for this section is 400 words.
- **Start date** – Please note the latest start date is 1 October 2024.
- **Duration** – Projects may be for up to 36 months in duration.

3.2 Core team

This section should include the roles that applicants have as the core team delivering the proposal. Please ensure all applicants are eligible to apply (see Table 2).

One applicant must be designated as the Project Lead, the second and any further applicants should be included as Project co-Lead(s) (UK) or Researcher co-Lead(s).

On occasions, it may be necessary to make changes to the core team between the formal outline and full application stage. If this is the case, please contact the NC3Rs Office for consideration.

Each application must include:

- Project Lead - Responsible for the intellectual leadership and overall management of the project (affiliated with the lead organisation).

OPTIONAL

- Project co-Lead(s) (UK) - Assists with project leadership and management, and may take over the leadership of the project if required (affiliated with lead or one of the collaborating organisations).

- Researcher co-Lead(s) - A research and innovation associate who is not eligible to be a project lead or co-lead, but who has made a substantial contribution to the formulation and development of the application and will be closely involved with the project. For example, a postdoctoral researcher working on the project.

3.2.1 Overseas researchers

Overseas researchers are not eligible to apply as Project Lead but can be included as collaborators or in **exceptional circumstances** as Project co-Lead (International). Project co-Lead(s) (International) must be approved by the NC3Rs Office prior to submitting an application. This approval must be mentioned in the Applicant and team capability to deliver section of the application form. More information on overseas Project co-Lead costs can be found in the MRC Guidance for Applicants. The NC3Rs has adopted MRC policy.

3.2.2 Researchers based in industry

Industry organisations are not eligible for FEC funding and are only eligible to apply for funding from the NC3Rs as a Project co-Lead. Alternatively, a researcher based in industry may be included as collaborator or Project partner.

3.2.3 Project partners

A Project partner provides a substantial intellectual contribution to the project, and their organisation may also provide resource either in-kind or financially. Project partners are not expected to request NC3Rs funding as part of an application. Details of Project partners and their contributions should be noted in the Project partners section of the application form. See section 3.9 for further information.

3.2.4 Collaborators

Details of collaborators should be noted in the Approach section of the application form and where relevant, letter of support provided. See section 3.4.2 for further information.

3.3 Vision

The **Vision** section should be a summary of what you aim to achieve with your proposed work. It should include the following information:

1. A description of the project's scientific and 3Rs objectives.
2. A rationale for how your proposed project:
    a. is of excellent quality and importance within or beyond the field(s) or area(s).
    b. is scientifically original and innovative.
    c. addresses a strategically important 3Rs area.
    d. has the potential to advance current understanding, generate new knowledge, thinking or discovery within or beyond the field or area of research.
    e. is timely given current trends, context and needs.
    f. may offer potential for additional health, socioeconomic or environmental benefits, and identify who the beneficiaries might be.

The word limit for the Vision section is **700 words**.

3.4 Approach

The **Approach** section should describe how you will deliver the proposed project. It is not necessary to describe each experiment, but enough detail must be provided to show how and why the research is competitive in the field and that it has been carefully planned to produce useful and reliable results.

Applicants should include:

1. **A comprehensive description of your experimental plans, including supporting preliminary data.** You should demonstrate how your approach:
    a. **is effective and appropriate to achieve your scientific and 3Rs objectives.** Highlight plans that are particularly original or unique.
    b. **uses a clear, transparent and sound methodology.** Robust methodology and experimental design should be at the centre of any proposal to ensure the reliability of results. Applicants are required to provide additional information on the proposal's experimental design and methodology (please see section 3.5 of the guidance).
    c. **is feasible and identifies potential risks to delivery and how they will be managed**. Applicants are encouraged to include a Gantt chart or similar.
    d. **if applicable, builds upon and progresses previous work.** If the project builds on previous NC3Rs funding, summarise the 3Rs impacts achieved to date.
    e. **will maximise translation of outputs into outcomes and impacts.** Consider how the model, tool or technology will be characterised or validated to show it is fit-for-purpose and has utility for potential end-users.
2. **A robust 3Rs case.** Please refer to section 3.4.1 for further guidance on writing a 3Rs case. In summary, this should include:
    a. a summary of how your proposed research will directly replace, reduce and/or refine the use of animals in research or testing.
    b. supporting metrics demonstrating the potential scale of the 3Rs impact.
    c. whether the outcomes could be applicable to other models or research areas.

3. **A dissemination strategy for sharing the proposed research and 3Rs outcomes with the wider scientific community, including the likelihood of adoption by other groups.** Clearly describe how 3Rs outputs will be shared with the wider scientific community to encourage and drive uptake, during the lifetime of your award and beyond (often termed the 3Rs legacy). Your dissemination plans should aim to achieve maximum 3Rs impact and be tailored to the 3Rs tool, method or technology. You should identify the end-users for the new model, tool or technology and highlight any advantages (3Rs or scientific) of the model, tool or technology that could improve uptake. In some instances, it is useful to include letters of support from the research community as a measure of the need for, and interest in, adopting the 3Rs model, tool or technology (see section 3.4.2 for further information). It may also be beneficial to describe other potential applications to further research areas. Consider any potential

barriers to uptake (for example technological challenges, access issues, cost, competition or regulatory) and how these may be overcome.

4. **A description of how your research environment (in terms of the place and relevance to the project) will contribute to the success of the project.** Explain how the research will benefit from the access to appropriate services, facilities, infrastructure, or equipment provided by the host institution or collaborating organisation(s).

Additional considerations may include:

- If the 3Rs model, tool or technology is developed successfully, what characterisation or validation is needed to assess whether it is fit-for-purpose? What, if any, additional steps will be required before it can be implemented within routine research? Include any plans with an industrial partner, if applicable, and provide details of their involvement in the project.
- 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 this forward? Any plans must be realistic and credible, and appropriate industrial links included.

Figures and images can be inserted into the Approach section, a descriptive legend should be included underneath each image. Figures and images must be less than 5MB and can be the following formats:

- JPEG, JPG, JPE, JFI, JIF, JFIF, PNG, GIF, BMP or WEBP

The word limit for the Approach section is **4500 words**.

References: relevant scientific publications may be cited in the Approach section of the application form. Numeric referencing style (in superscript) should be used within the body of the text and a complete list of citations included in the References section of the application form. The word limit for the References section is **500 words**.

3.4.1 Writing a 3Rs case

It is important to effectively articulate the potential 3Rs impact of your proposed work, including providing realistic metrics, so the Panel can assess your application against others in the competition. Proposals are evaluated equally on the quality of the science and the likely 3Rs impact should the proposed research be successful.

When writing your 3Rs case, consider the following questions:

- Why is this project important to the 3Rs?
- Which ‘R’ is the project targeting?
- Why is the 3Rs impact potential realistic and achievable?

This 3Rs case should include metrics on the potential 3Rs impact locally (e.g. within your own laboratory or institution) and more widely (nationally/internationally). It can be difficult to provide a specific estimate for 3Rs potential as it is not always straightforward to identify how many animals are used for a certain procedure/experiment/discipline, on a national/international scale. Nevertheless, your application should describe a reasonable estimate of the 3Rs potential and how you arrived at this figure.

A logical approach should be taken to estimating the 3Rs potential of your project and it is often useful to start locally from your own experiences and then extrapolate to the wider scientific community. What 3Rs impacts could be made in your own laboratory, in this project and in future projects, as a result of receiving NC3Rs funding? Could this be expanded to other researchers in your institution? Seek input from colleagues and researchers in relevant fields based on their experiences. Evidence based on laboratory or institutional usage can provide a starting point to make the impacts easier to quantify and build up the 3Rs rationale of the project.

We recommend considering the following questions:

1. **For replacement:** describe the types of animal models and studies (and their level of severity on the animals) that could be replaced and the numbers of animals currently used for this purpose. What proportion of this use could be replaced if the proposal was successful, and how have you arrived at this estimate?

2. **For reduction**: describe the current experimental groups or number of animals that are used in a study and what this would be reduced to if the proposal were successful.

3. **For refinement:** describe the nature and level of suffering the animals may experience, including the number of animals that experience this suffering, and how this would be minimised if the proposal was successful. Include evidence that animal suffering will be reduced, or animal welfare improved and describe the objective indicators that will be used to assess animal welfare. Consider whether the severity limit for the procedure or protocol is likely to be downgraded as a result of the proposed refinement technique and estimate how many animals are likely to benefit per year, both locally and in the wider scientific community.

Applicants may also supplement their 3Rs case with information gathered from literature databases (such as PubMed). For example, 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. This can be a useful exercise in estimating potential global impact and should be used to **support** information from your own laboratory or institution, from collaborators and/or other end-users.

The NC3Rs publishes summaries of its funded grants on the NC3Rs website. Please ensure the Vision statement is suitable for web publication if an award is made.

For further guidance on how to clearly convey the potential 3Rs impact of your work, please use our resource: ‘How to write effectively about the 3Rs in your grant application’.

3.4.2 Letters of support attachment

If applicable, please upload relevant letters of support as a **single** attachment in the Approach section. Letters of support should be from collaborators based in academia or industry who may be providing scientific expertise, resources and/or training, or who are interested in adopting the 3Rs model, tool or technology should be included in the attachments. Letters of support 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.

The file should be in PDF format and the size must not exceed 8MB.

3.5 Experimental design and methodology

Applicants are required to clearly describe and justify the experimental design and methodology of the proposed research. This includes, as appropriate:

Objective and general approach

- Specific hypotheses being tested.
- Brief details of the design of each experiment, including the groups being compared.

Sample size

- The proposed sample size per group, along with a clear definition of the experimental and biological units.
- How the sample size was calculated, showing power calculations and including justification for the effect size chosen. Consider any risks associated with not achieving the sample size required.
- If power calculations are not appropriate, justify why and provide a principled explanation of the choice of sample size. Explanations based solely in terms of ‘usual practice’ will be considered insufficient.
- If using animals, total number in each experiment

Measures to reduce subjective bias

- How masking (blinding) will be implemented or why it is not appropriate.
- How randomisation will be carried out or why it is not appropriate; how the sex will be taken into account in the allocation to experimental groups.
- Inclusion and exclusion criteria. Also consider potential sources of sampling bias in both field and captive studies with wildlife species.

Outcomes measures and analysis plans

- Outcome measures that will be assessed. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.

- Analysis plans, explaining how sex and other factors are taken into account and showing that statistical methods are appropriate for the types of data that will be collected.
- Details of any statistical advice sought/available.

Animals/samples characteristics

- The sex of the animals, humans, tissues or cells to be used in the study. If the sex cannot be determined, provide a justification for this. If the proposed study is not using both sexes, provide a justification.
- Relevant information for the samples, animals or model organism to be used (e.g. species, strain, developmental stage, weight).

This information is provided as mandatory appendix; there are two possible formats:

Applicants must include an appendix, using one of the following options:

- EDA Report – only for experiments using animals (see section 4.2)

- Experimental design and methodology appendix. This is limited to one side of A4. The purpose of the appendix or EDA report 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 **Approach** section. Applicants should not duplicate information presented elsewhere in the application.

  Where appropriate, the use of figures, tables and/or diagrams is encouraged. The appendix should be uploaded as a PDF file in the Experimental design and methodology section. The file size should not exceed 8MB.

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.

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.

3.6 Applicant and team capability to deliver

In this section, applicants are required to provide a narrative in the format of the Résumé for Research and Innovation (R4RI). The purpose of the narrative is to showcase the skills and expertise of the proposed research team, and how this will help successfully deliver the proposed project.

In your R4RI statement, provide evidence of how you, and if relevant your team, have:

- The relevant experience (appropriate to career stage) to deliver the proposed work.
- The right balance of skills and expertise to cover the proposed work.
- Where applicable, a track record in implementing the 3Rs in your research and disseminating research outputs and impacts.

The word count for this section is **1500 words**, 1000 words to be used for R4RI modules and, if necessary, a further 500 words for Additions. Include a response for the whole supervisory team. You should consider how to balance your answer and, where appropriate, emphasise the key skills each team member brings. See the UKRI guidance on R4RI for further information. The five R4RI module headings are listed below:

- Contributions to the generation of new ideas, tools, methodologies, or knowledge.
- The development of others and maintenance of effective working relationships.
- Contributions to the wider research and innovation community.
- Contributions to broader research or innovation users and audiences and towards wider societal benefit.
- Additions – Where relevant, we encourage applicants to use this section to provide any factors which may give context to your R4RI statement. For example, details of career breaks if you wish to disclose them – it is not a requirement.

You may demonstrate elements of your responses in visual form if relevant. A descriptive legend should be included underneath each image. Figures and images must be less than 5MB and can be the following formats:

- JPEG, JPG, JPE, JFI, JIF, JFIF, PNG, GIF, BMP or WEBP

If applicable, where an overseas researcher is included as Project co-Lead (International), please also mention whether prior approval by the NC3Rs Office has been sought.

The word count for this section is **1500 words.**

3.7 Ethical information

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

3.8 Resources and costs

In this section, applicants are required to summarise and justify the resources needed to achieve the objectives of the project.

3.8.1 Resource summary

Please enter the costs being requested under the relevant headings (see Table 3 for further information).

Points to note:

- Costings should be calculated on the basis of full economic costs (FEC). The NC3Rs will generally meet 80% of these costs unless there are Exceptions.
- All fields in the Resources section must be populated, even if nil costs apply.

Additional guidance on completing the Resources section can be found in the MRC Guidance for Applicants with specific guidance regarding the costing of equipment onto a proposal.

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 3.8: Costing of applications involving MRC institutes, when completing their application.

Industry investigators are eligible for 100% directly incurred costs only, which should be entered in the Exceptions section with further explanation included in the justification for resources.

Equipment costs

- Single items of equipment costing less than £10k should be included in Other Directly Incurred costs, rather than under the Equipment heading.
- 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.
- Please contact the NC3Rs Office where items of equipment will exceed £138k (£115k excl. VAT). A business case (limited to two sides of A4) is required for outlining the strategic need for the equipment (see UKRI website for further information).

Table 3: High-level cost headings

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 Research Councils will fund in full (e.g. at 100%), subject to actual expenditure incurred, or items that are outside FEC. 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 value for items of equipment over £10k and so only the amount requested from NC3Rs should be entered. Costs related to industry investigators should be included under this cost heading.

3.8.2 Justification for resources

The purpose of the justification for resources is to aid assessors in making an informed judgement on whether the resources requested are appropriate for the proposed research.

For some items it is not necessary to justify the monetary value, rather the type of resource, such as amount of time or type of staff requested.

In particular, justify the following resources:

- Project staff.
- Animal costs.
- Any equipment that will cost more than £10,000.
- Any consumables beyond typical requirements, or that are required in exceptional quantities.
- All facilities and infrastructure costs.
- All resources that have been costed as 'Exceptions'.

Costings should be justified on the basis of full economic costs (FEC) of the project, not just on the costs expected from the NC3Rs. It is important to demonstrate how the resources you anticipate needing for your proposed work:

- Are comprehensive, appropriate and justified.
- Represent the optimal use of resources to achieve the intended outcomes.
- Maximise potential outcomes and impacts.

For more information on completing the justification for resources document please see the MRC Guidance for Applicants.

The word limit for this section is **1000 words**.

3.9 Project partners

Where an application includes project partners, provide the following information:

- Details of each project partner.
- Whether each project partner is making a direct or indirect contribution to the project (see Table 4 for further information).
- The monetary value of the contribution.
- An explanation for why project partner contributions are important for your project.

Table 4. Project partner contributions

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.

3.10 Data management and sharing

The NC3Rs has adopted the MRC policy on data management and research data sharing. A Data Management Plan (DMP) that clearly details your project's approach to managing data should accompany your application. Complete the template DMP and upload as a PDF file (maximum file size should not exceed 8MB). The notes in the template (*in italics*) provide further context and guidance for completion.

The DMP should describe:

- How your approach to managing data is appropriate for the research project being proposed.
- How the DMP will enable the project's data creation, outputs and storage needs.
- How the plan for data is feasible, sensible, appropriate and valid.

The DMP is assessed by peer reviewers alongside the rest of the application. 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**.

4. Use of animals

Over the past few years there have been a number of important initiatives aimed at raising the 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 outlined here will require additional resources, e.g. for 'chipping' animals or costs associated with obtaining statistical support. The NC3Rs recognises this and such costs should be fully justified in the appropriate sections.

4.1 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 'Experimental design and methodology' section of the application form why using both sexes is not appropriate or possible.
- type of animal(s), for example, strain, pathogen free, genetically modified or mutant.

4.2 Experimental design, minimising subjective 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 highlighted in section 3.5.

Applicants using animals in their research are strongly encouraged to design their experiments using the Experimental Design Assistant (EDA) and use an EDA report to provide the requested methodology and experimental design information (see section 3.5).

The EDA captures methodological details about the experimental plan in the form of a diagram and provides tailored guidance and feedback on the design. Each EDA diagram represents one experiment and only **one EDA report** can be used per application. The report included could represent the main experiment of the grant, a representative experiment, or the experiment that will use the largest number of animals. Applicants can use the text box (max 300 words) to provide context or add information not contained in the EDA report, for example a justification for not using both sexes.

The Panel assessing applications will assume experimental design principles used in the experiment presented in the EDA report (e.g. randomisation to allocate to groups) will be used in all applicable experiments in the grant. The complete report must be included in your application, and the tables and EDA diagram must not be altered on the PDF. If you need to update the EDA report, update the EDA diagram online and generate a new report.

4.3 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 5.

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 Approach section, will be subject to

equally careful scrutiny, and will carry substantial weight when assessing the scientific strength of the proposal.

Table 5: Information required within the application form

TFS section: Experimental design and methodology	The experimental design should be outlined in the experimental design and methodology section, including the information listed in section 3.5. In general, it would be expected that professional statistical advice will be sought in putting this section together. It is essential that the case is clearly made as to how the chosen design will enable the stated objectives of the study to be achieved. 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.
TFS section: Research involving the use of animals	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. Using the template in the Research involving the use of animals 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. Applications including the use of higher species **(including non-human primates, cats, dogs, pigs or equines)** will undergo an additional review by the NC3Rs Office to ensure the usage is fully justified and that the welfare and husbandry standards are optimal. The information provided in this template is used for this purpose; therefore it is imperative all the questions are fully addressed.
TFS section: Conducting research with animals overseas	This section must be completed for all proposals involving animal research that will be conducted overseas. Applicants are required to:

	1. Provide a statement that confirms that they will: ▪ adhere to all relevant national and local regulatory systems in the UK and overseas. ▪ 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. ▪ have appropriate national and institutional approval in place before initiation of the proposed animal work. Successful proposals may be expected to provide copies of these permissions before funding is released. 2. Complete and upload the relevant checklist based on the species of animal(s) to be used. Additional guidance on conducting and reporting animal research can be found on our Peer review and advice service hub.
TFS section: Resources and costs	**Costs:** The costs of both the animals themselves and their maintenance may be requested and should be listed in the Resources and costs section. 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. **Justification for resources:** A detailed justification of the costs incurred for breeding, maintaining and using the chosen number of animals should be given in the justification for resources section (see 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 'Experimental design and methodology' and 'Research involving the use of animals' sections of the application form. Where experiments involve genetically altered animals, examples of the breeding strategies should be included to support the total number of animals requested. 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.

4.4 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 page 14 of Responsibility in the Use of Animals in Bioscience Research).

4.5 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.

4.6 Mouse strains

The NC3Rs encourages the archiving and sharing of genetically altered mouse strains as a means of both reducing and refining animal use[1]. 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

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

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.

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

5. Submitting an application

When all sections of your application are complete you must send it to your research office for approval; this is done via TFS. This enables institutional checks to be carried out before final submission to the NC3Rs. Please allow appropriate time (**a minimum of five working days**) before the submission deadline for these checks.

The research office then submits the application to the NC3Rs for assessment.

6. Assessment procedure

There is a two-stage application process for project grant applications. The first stage is the formal outline application which is assessed by the Grant Assessment Panel. The Panel will reach a consensus decision for each application on whether or not the applicant should be invited to submit a full project grant application.

In the second stage, invited full applications will be sent for external peer review. In making final funding recommendations, the Grant Assessment Panel will consider both the full application and comments from the external peer reviewers.

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

- Potential impact on the 3Rs.
- Quality of the proposed project.
- Current or future importance of the proposal to medical, biological or veterinary science.
- Strategy for promoting the proposed research and 3Rs outcomes within the scientific community.
- Expertise and track record of the team.
- Value for money.
- Strategic relevance (where appropriate).

The NC3Rs website has further information available, including the assessment and scoring criteria for Panel members, Panel membership and Declarations of Interest.

Please note Panel decisions are final and not open to appeal.

All applicants will be informed of the outcome of their full application after the Panel meeting in July.

The NC3Rs reserves the right to amend the application process.

6.1 Reviewers

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.

Reviewer nominations and exclusions should be saved as a PDF and sent to the NC3Rs Office by email after your application has been submitted.

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 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.

6.2 Applicant response to external peer reviewers' comments

Following external peer review there is an opportunity for applicants 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.

7. 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.

7.1 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 the current NC3Rs Grant Assessment Panel can be found on the NC3Rs website.

7.2 What we publish on our website

Details of awarded grants are routinely published. The information published on the NC3Rs website includes the following:

- Grant holder names, including co-applicants.
- Host institution and location.
- Value and duration of award.
- Research project title.
- Vision statement.
- 3Rs and research classification.
- Potential 3Rs impact.
- Keywords.
- Grant associated publications and other outcomes.

7.3 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 information is handled appropriately and any sensitive material is correctly identified and has 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.

8. 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.

Information on Post Award processes (including grant extensions, requests for suspensions and transfers) can be found on the NC3Rs website.

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.

8.1 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.

Project grant award holders must abide by the Terms and Conditions of UKRI Research Grants.

8.2 Publications and Open Access publishing

The NC3Rs has adopted 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 all outcomes of NC3Rs-funded research including 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 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 (e.g. 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.
- Report animal-based studies in accordance with the ARRIVE guidelines; this includes studies using non-mammalian model organisms.

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 3rsgrants@nc3rs.org.uk 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 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.

8.3 Reporting requirements and evaluation

Information on the outcomes of NC3Rs 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 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 3: 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. ▪ The NC3Rs has an annual collection period in line with the Research Councils. ▪ 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.

8.4 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.

8.5 Mid-award and end-of-award progress reports and meetings

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

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.

9. Useful links and resources for compiling an application

9.1 Websites

- NC3Rs website
- NC3Rs Project grant scheme
- UKRI Funding service homepage
- How to make a successful grant application
- UKRI Research Grants Terms and Conditions
- Researchfish
- Experimental Design Assistant

10. Questions and queries

For questions related to the Project grant scheme please contact the NC3Rs Office: 3rsgrants@nc3rs.org.uk

For questions related to the use of the Funding Service, please contact support@funding-service.ukri.org or call the UKRI Funding Service Helpline: +44 (0)1793 547 490

Appendix – Project pipeline definitions and examples

The NC3Rs funds multidisciplinary research to provide 3Rs models, tools and technologies that scientists in academia and industry can use to answer important questions to generate new knowledge, improve human and animal health and protect the environment. Our goal is to provide 3Rs models, tools and technologies that are well-characterised and ready for deployment and importantly are better than existing approaches in terms of their predictivity, reliability, reproducibility, cost and impact on animal welfare. To do this we provide funding to support the initial development of 3Rs approaches, their characterisation to demonstrate that they are fit-for purpose and sharing across the wider community to encourage uptake and their use into routine practice. We refer to this as our project pipeline – there are four steps in the pipeline which are detailed below. Our funding schemes map across the pipeline as shown in Table 1.

Development: Creating new models, tools and technologies to deliver 3Rs impact

This is the first step in the pipeline focusing on building a new 3Rs model, tool or technology to address an important scientific question, new challenge or bridge a key knowledge gap where there is a clear 3Rs need. The emphasis is on developing an approach that does not already exist and that has potential for achieving significant 3Rs impact.

Projects may focus on creating an entirely novel 3Rs model, tool or technology; bringing together different approaches or opportunities to establish a new 3Rs model, tool or technology; or substantially modifying an existing model, tool or technology where there is significant and unrealised 3Rs potential.

Studies should aim to generate evidence to support the proof-of-concept. An important focus should be on determining whether the proposed 3Rs approach is feasible and providing important data to help further develop and build the 3Rs model, tool or technology.

Examples include: Development of a new invertebrate model of disease as an alternative to the use of vertebrate approaches; increasing the complexity of a microphysiological system by including additional elements such as flow or other cell types; or modifying an existing *in vivo* procedure to reduce the number of animals required per study or improve welfare outcomes.

Fit-for-purpose: Building confidence in 3Rs approaches within the context of use

This part of the pipeline focuses on generating an evidence base to demonstrate that the 3Rs model, tool or technology is appropriate for the intended scientific purpose and will have an impact on the use of animals.

Studies should demonstrate the 3Rs model, tool or technology is relevant, reproducible and scientifically robust, and may encompass the following:

- Detailed model characterisation (conceptual validation) to demonstrate the distinctive features and performance characteristics of the 3Rs approach. For example, this may include studies to determine the biochemical, histological, pharmacological, genetic and functional profile of a model.

- Feasibility studies that build on the proof-of-concept data to show the validity and utility of the 3Rs model, tool or technology. These studies may focus on determining whether the 3Rs approach is performing as expected, is generating results that are relevant and is appropriate for further testing to address a specific research question or purpose.
- Optimisation studies that further fine-tune the model, tool or technology to improve its utility.
- Comparative studies to demonstrate how the 3Rs approach is scientifically better than, or at least comparable to, currently used methods to help build confidence in the model, tool or technology. Studies often include a like-for-like comparison against the current state-of-the-art or gold standard animal models, or benchmarking against historical animal data or clinical data.
- Reproducibility studies to show that the 3Rs model, tool or technology produces reliable and replicable findings, helping to build further confidence in the approach. Studies may focus on replicating findings at the experimental level such as between different strains of animal, species or cell lines; or at an operational level such as between users within the same laboratory or between different laboratories.

Dissemination: Promoting 3Rs approaches to the wider scientific community

This part of the pipeline focuses on sharing research findings with the scientific community, to achieve wider awareness of and engagement with the 3Rs model, tool or technology.

The communication and dissemination of a 3Rs approach is an essential factor in achieving wider 3Rs and scientific impacts, as these can only be delivered if an approach is adopted by others. Dissemination activities should be focused on different ways of sharing a 3Rs approach that ideally go beyond publications and conference attendance, to help lay the foundations for building a lasting impact that continue after the lifetime of an award. For all publications, open science practices are encouraged and reporting guidelines, including ARRIVE, should be followed to better enable others to evaluate and reproduce the 3Rs approaches and associated scientific findings.

Examples include: General grant outputs such as publishing methods articles, including on the NC3Rs gateway, that provide the full experimental details for setting up the model, tool or technology and research articles focused on using the 3Rs approach; presenting the 3Rs approach at key scientific meetings/conferences; delivering training or practical workshops to raise awareness of the 3Rs approach; or developing online resources, including videos, to aid further dissemination of the 3Rs approach.

Uptake and impact: Accelerating the adoption of 3Rs approaches into routine practice

The final part of the pipeline focuses on actively transferring the 3Rs model, tool or technology to new end-users that will have a direct and immediate impact on the 3Rs. The objective should be to build further confidence in the 3Rs approach, within the context it is being used, to realise the maximum scientific and 3Rs potential. Facilitating the adoption of 3Rs approaches by transferring the “know-how” so that the model, tool

or technology is used by other researchers is key to sustaining lasting 3Rs impact well after an award has ended.

Examples include: Establishing new partnerships or collaborations with the primary aim to deploy the 3Rs model, tool or technology into more laboratories/research settings; studies demonstrating the portability or transferability of the 3Rs approach to a new setting or research field/question.

Figure 1: NC3Rs Funding schemes mapped onto the project pipeline