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

How to write effectively about the 3Rs in your grant application

While the focus of this guidance is for those preparing applications, the principles also apply to communicating information on the 3Rs when delivering presentations and posters at conferences, when writing publications, as well as during public engagement activities.

Communicating effectively and accurately how your proposed research will achieve a 3Rs impact is essential for securing funding. Applications submitted to the NC3Rs are assessed on their potential 3Rs impact as well as the quality of the underpinning science and technology. It is important your application clearly articulates the estimated 3Rs impacts, including providing realistic metrics, so that the funding panel can assess your application against others in the competition.

To assist researchers applying for NC3Rs funding in clearly conveying the potential 3Rs impact of their work, we have developed the guidance below. The key topics to consider have been grouped under two headings, focus and rationale. Focus predominantly covers the importance of the 3Rs potential (including how a 3Rs legacy will be achieved) and rationale how to estimate the 3Rs impact.

The 3Rs should be embedded throughout your grant application, from the Je-S proposal form through to the additional attachments. For further information on the application process for NC3Rs funding schemes please refer to the NC3Rs Applicant and Grant Holder Handbook.

Focus

The focus should primarily be the 3Rs potential of the project. Consider:

Why is this project important to the 3Rs?

It is important to set out the benefits of using your proposed 3Rs model/technique/technology compared to current methods. For example, do the established animal models used in your field involve procedures associated with a high degree of suffering or is there a high level of variability in the animal model such that large numbers of animals must be used to get meaningful data? Or do the animal models have scientific limitations for example, show poor translation to humans? You should detail what species of animal will be affected by your project and whether your findings are potentially relevant to other species or procedures.

Which ‘R’ is the project targeting?

You should make it clear which ‘R’ your project is targeting, taking care to ensure you select the correct definition. In some circumstances a proposal may focus on more than one of the ‘Rs’, which should be reflected in the potential 3Rs impacts.

How is the model/technique/technology going to be characterised or validated?

It is important to describe how you will demonstrate your new approach is scientifically better than, or at least comparable to, currently used methods to promote the uptake of your model/technique/technology within the scientific community. In many cases, this will involve a comparison with historic animal data or conducting comparative studies and you should explain why this is the best approach for characterising your model/technique/technology. Where there are concerns about the limitations of the established methods (e.g. poor relevance to humans) you should consider whether a more robust characterisation or validation could be achieved by comparing your model to clinical data instead.

What barriers to uptake could there be?

It is important to describe what barriers might affect the uptake of the new 3Rs approach by your peers and the wider scientific community. Identifying these barriers can help in understanding why there may be resistance to the new model/technique/technology. You should set out in the application how you could help address the barriers, as this demonstrates a thorough understanding of both the project and the limitations influencing the potential 3Rs impacts.

Who are the end-users for the new model/technique/technology?

Maximising the 3Rs impacts that can be delivered is dependent on achieving a long-term 3Rs legacy. You should describe who the end-users of your model/technique/technology are and how you have engaged, or plan to engage, with them to disseminate your 3Rs impacts and encourage wider uptake. Ideally, you should provide letters of support to demonstrate that you have the right networks.

Are there any advantages (3Rs or scientific) of the model/technique to highlight that could improve uptake?

Highlighting additional scientific advantages informs the community of non-3Rs related benefits of the new model/technique and can help to drive uptake. For example, an *in vitro* replacement technique may offer additional benefits beyond the reduction in animal use, such as giving a better understanding of molecular mechanisms. Whilst this would not be a 3Rs impact (since the molecular mechanisms could not be analysed easily in animals) it is a scientific advantage of using the replacement technique that should be articulated.

Rationale

The potential 3Rs impact of a project is impossible to define or assess without providing metrics with a clear justification. Consider:

What types of metrics should be provided in your application?

It can be difficult to provide a very 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. It is important not to provide sweeping generalisations such as “this project will reduce the use of millions of animals in toxicology” or “this model could replace up to 20% of patient-derived xenograft mice in cancer studies”.

Instead, start locally from your own experiences. 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. More specifically:

> **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 that are 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?
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> **For reduction**: describe the current group sizes or number of animals that are used in a study and what this would be reduced to if the proposal were successful.
>
> **For refinement**: describe the nature and level of suffering that the animals may experience, including the severity of the model and how many animals experience this suffering, and how this would be minimised if the proposal was successful.

Applicants often use reference depositories (such as Pubmed) to estimate a global 3Rs impact. Whilst a useful exercise, it is difficult to judge from these metrics alone the potential scale of 3Rs impact and it is important to supplement this with information from your own laboratory or institution, from collaborators and other end-users.

In most cases, the annual Home Office statistics on animal use under the Animals (Scientific Procedures) Act 1986 do not provide suitable estimates of potential 3Rs impact for grant applications. The information provided is too broad (for both animal numbers and the level of suffering) as predominantly research proposals focus on a specific model, procedure or technique. For example, the statistics give the total number of animals used in “human cancer” research. This figure will encompass a wide range of animal models for various types of cancer and different research questions; it is unlikely that any 3Rs proposal could have an impact across all of this. The exception would be a proposal that could affect large numbers of animals across a range of disciplines, as is the case for the work to refine mouse handling for example, where it would be reasonable to anticipate a broad impact.

Why is this 3Rs impact potential realistic and achievable?

Why are you confident your project can achieve the predicted 3Rs potential? Is this based on personal experience using the animal models and the types of questions that you investigate using them that could now be explored with the 3Rs model/technique/technology? Or, have you contacted other potential end-users of the model to confirm how many of their experiments could be influenced by your project?

Where you are applying for 3Rs funding but do not use animals in your research you should ensure you have consulted with potential end-users of your proposed 3Rs model/technique/technology to provide a reasonable estimate of the impact. It is advisable in this case to also include letters of support as part of your application.

Project specific examples

You may find it helpful to look at project specific examples, which can be found in the overviews written for the ‘Our Science Pages’. Whilst a grant application requires a greater level of detail

than an overview contains, the overviews demonstrate how to approach building a 3Rs case with supporting metrics. Specifically, the 'Why we funded it' section provides a short summary of the 3Rs impact potential of the awarded grant. We have highlighted three exemplar projects, which demonstrated clear metrics and a well-thought out justification in their applications making them good examples for how to include metrics to support 3Rs impacts, and this is reflected in the 'Why we funded it' section of each project.

Replacement: Replacement of animals in cancer drug development by using 3D in vitro functional assays for increased predictive power

Reduction: Validating a sexual development test using the 3-spined stickleback for addressing the 3Rs in fish toxicity testing

Refinement: Improving biological integration of osseous and dermal tissues in macaque cranial implants