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

Developing and implementing an institutional 3Rs strategy

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Pioneering Better Science

The NC3Rs is a UK-based organisation that works with scientists across the biosciences sector (nationally and internationally) to develop and implement technologies and approaches which replace, reduce or refine (the 3Rs) the use of animals in research and testing. It is the UK's main funder of 3Rs research and innovation and in addition has a small team of scientific staff who lead activities to embed the 3Rs in policy, practice and regulations. The NC3Rs has an annual budget of approximately £10 million with the core funding provided by the MRC and BBSRC, with additional support from Government departments, research charities and the pharmaceutical, chemical, agrochemical and consumer product industries for specific posts, projects and funding calls.

Further information can be found on our website: www.nc3rs.org.uk.

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Introduction

The NC3Rs has previously published an institutional framework for the 3Rs (nc3rs.org.uk/institutional-framework-3rs) that comprises seven related principles, including the importance of taking a strategic approach to embedding the 3Rs in local policies and practices. Here we provide details on how to develop and implement a 3Rs strategy from identifying priority areas through to measuring impact.

1. Many research organisations working in the bioscience sector have a public statement on their use of animals and commitment to the 3Rs. The goal of this commitment should be two-fold; first to ensure that any use of animals is fully justified and genuinely conducted to the highest standards, and second to facilitate active participation in the development of new 3Rs approaches that support robust, reproducible and humane research with benefits for human health, protection of the environment and animal welfare.

2. Delivering these goals requires the 3Rs to be embedded in the culture, research priorities, policies and practices of the organisation – fully achieving this is dependent on a coordinated and comprehensive strategy that focuses on leadership, infrastructure, people and training as well as the allocation of appropriate resources. At a high level the 3Rs strategy should lead to:

    - Visible ambition across the organisation and at all levels to advancing the 3Rs.
    - Individual behaviours and actions that reflect an understanding of the importance of the 3Rs to high quality science and ethical research.
    - A sustained and measurable impact on animal use and welfare.

3. The purpose of this document is to support research organisations to develop and implement a strategy that has widespread engagement and buy-in. The information and ideas included are intended to inspire action, aid discussion, and illustrate what is possible. Throughout, the phrase 'research involving the use of animals' is used to refer to:

    - The use of animals in scientific procedures covered within the scope of national legislation, for example, work regulated under Animals (Scientific Procedures) Act 1986 in the UK, or its equivalent worldwide (such as Directive 2010/63/EU or the Animal Welfare Act in the USA).
    - The use of animals for research purposes not regulated by legislation on scientific procedures (e.g. behavioural observations; capture, mark and release of wildlife; and veterinary clinical research).
    - The use of stock animals to generate, breed or maintain the supply of animals for research purposes.
    - The use of animal-derived products and/or research materials/data (e.g. from commercial sources, abattoirs, zoological or museum collections, animal welfare/wildlife projects or veterinary clinical practice).

4. This document is primarily for use by those who are involved with overseeing and managing the use of animals in the organisation. Information is divided into the following sub-headings:

    - Who should be involved?
    - Implementation plan
    - Resources required
    - Indicators of success

Developing a 3Rs strategy

5. The first step in the development of a 3Rs strategy is to decide what your research organisation's long-term or overall vision is. Often this is the most challenging step, especially if the intention is to develop a 3Rs strategy that will influence behaviour and deliver cultural change on the use of animals. Strategies work best when they are introduced into a supportive environment that is open to change. Ideally there should be collective responsibility for the development, delivery and implementation of the 3Rs strategy, with clear expectations of what staff will be required to do. It is important that members of the senior management team are actively involved throughout so they can lead by example rather than delegating responsibility to others around them, as well as assign resources and budget.

6. There is no 'one size fits all' approach when it comes to developing and implementing a meaningful 3Rs strategy. The approach taken should be influenced by various factors including the number and type of research projects involving the use of animals that are being undertaken and/or planned at the organisation and the existing level of support across scientific and technical staff for implementing the 3Rs. It can be helpful to focus initially on what is easily achievable whilst formulating an innovative plan for progressively more challenging and longer term aims.

7. To start the process of developing an effective 3Rs strategy it is helpful to:

    - Discuss the concept of a 3Rs strategy with senior leadership including the Vice Chancellor, Chief Executive Officer or equivalent, as well as the Animal Welfare and Ethical Review Body (AWERB) or Institutional Animal Care and Use Committee (IACUC), and other relevant 3Rs, animal welfare, research management, research governance and strategy committees.

    - Review the use of animals in your organisation (e.g. numbers, species, types of procedures/protocols, scientific disciplines), including recent trends, to provide a baseline for measuring impact and to help inform your priorities and use of resources. Ideally, the review should capture as far as possible future research directions and other external influences (e.g. regulatory change) that may affect animal use and/or the 3Rs.

    - Conduct a 3Rs self-assessment using the tool provided by the NC3Rs (3rsselfassessment.nc3rs.org.uk) to review how well the 3Rs are currently supported and implemented at your organisation, and inform your priorities for the strategy and use of resources. Aligned with this, it can be helpful to conduct an organisation-wide survey to identify 3Rs opportunities relevant to different groups as this ensures early engagement and buy-in, helps identify topics of common interest and can support the prioritisation of objectives.

    - Review different approaches to implementation of the 3Rs taken by other organisations and published on their websites or within the scientific literature (note the NC3Rs institutional 3Rs self-assessment tool provides examples of 3Rs initiatives from other organisations as part of its feedback function).

    - Consider which individuals and/or groups will be essential to the development and delivery of a 3Rs strategy and how they might be involved in the process.

8. Rather than deciding on a generic goal of improving implementation of the 3Rs, the strategy should focus on specific objectives for each of the 'R's or tackling specific 3Rs challenges faced within the organisation. It is important to consider from the outset what evidence or data you can collect to monitor and track progress in the delivery of your objectives. Wherever possible this should initially be linked to data that is already recorded, tracked, or monitored. Plans can subsequently be developed to collect additional data as appropriate.

9. The strategy needs to be ambitious but realistic and reflect the position that your organisation is starting from. Ideally, the strategy should be referenced within your institution's policy on animals and be publicly accessible. It makes sense to develop a strategy that aligns with the organisation's broader vision or values. Linking your 3Rs strategy to an externally-driven initiative, such as the bioscience sector's focus on improving research integrity or tackling the reproducibility crisis can be helpful for its delivery and gaining support.

10. Defining a timeframe for change can be an effective way to provide positive motivation whilst the strategy is a 'work in progress'. It is especially helpful for long-term goals that can be broken down into discrete steps to make the overall aim feel more achievable or accessible. For example, if the goal is to improve the experimental design and analysis of all animal studies conducted at the organisation, an initial first step could be to ensure that all first year PhD students doing *in vivo* studies are provided with dedicated training using the NC3Rs Experimental Design Assistant (eda.nc3rs.org.uk).

Who should be involved?

11. It is essential that ownership of the 3Rs strategy and accountability for its overall delivery is given to an individual at a high level within the organisation. Responsibility for doing the work to deliver each objective within the strategy should be assigned to a group of individuals or committee as appropriate, ideally with a single individual nominated as accountable for signing off that the objective has been completed. Progress reports should be published regularly, and where appropriate, be publicly available to ensure transparency and ongoing engagement with staff.

12. Within every research organisation there will be individuals who have extensive experience of strategy development and implementation. The process of developing a 3Rs strategy is a great opportunity to connect with and utilise expertise within the broader organisation. For example, you may find individuals with the skills and experience required to develop and implement a new strategy (including experts in project and change management) within research governance, business, or human resources departments. Having a 3Rs strategy can also provide the opportunity to enhance cross-disciplinary collaboration and utilise expertise available within other departments such as mathematics or engineering, which, although not traditionally associated with animal research, can provide important scientific and technical input into the development of 3Rs approaches, particularly those focused on replacement. Involving individuals who are external to the organisation can also provide a valuable independent perspective.

13. Staff expected to be involved in the delivery of the 3Rs strategy, including collecting and providing metrics on impact, should have the opportunity to contribute to its development. This should include staff of different seniorities and career stages (including early career researchers) and from different parts of the organisation including:

    - Committee members – for example, senior management, ethical review, 3Rs, animal care and use, strategy and research governance.
    - Named persons in the UK – for example, the Establishment Licence Holder, Named Animal Care and Welfare Officer and Named Training and Competency Officer.
    - Animal facility staff – for example, animal technicians, team leaders, research support/ managers and veterinarians.
    - Researchers whose work involves the use of animals, as well as those specialising in technologies with replacement potential (e.g. *in vitro* models, artificial intelligence, material sciences).
    - Administrative staff with responsibilities for managing grant funding or purchasing research products and materials that may be derived from animals (e.g. antibodies).

14. There are often many individuals in the organisation, either in the laboratory or animal facility, who are actively engaged in the 3Rs, albeit not usually in a coordinated way. These "3Rs champions" are a useful cohort for including in the development of the strategy and may be able to fulfil an ambassadorial role in terms of communicating its purpose and impacts. It is worth considering whether the role of 3Rs champion should be formalised as part of the strategy, for example, allocating the role to a nominated post-doctoral researcher in each department (or by research group) and to a nominated technician in each animal facility. This could be a development opportunity for the individuals concerned and recognised as part of the appraisal process.

15. It is advisable to plan from the start how and at what stages the views of different individuals will be collated, considered, and used to inform the development of the 3Rs strategy. Get this step right and the participation of staff with the final 3Rs strategy will be significantly enhanced. Ideas for engagement include:

    - Conducting a survey to review how well individuals are currently supported to implement the 3Rs, and/or gather opinions on what could be done better and how.

    - Asking for nominations or randomly selecting individuals from different peer groups to attend in-person or virtual workshops to discuss what areas the 3Rs strategy should prioritise.

    - Setting up an email account, or internal post box and encouraging staff to share their thoughts on the individual objectives included, or the long-term goal of the 3Rs strategy.

    - Using the local animal ethics committee, 3Rs champions and/or NC3Rs Regional Programme Managers (as applicable) to act as a focal point for engagement and communication activities.

16. The strategy should be unambiguously worded with clear objectives that state what it is as an organisation you are committing to achieving and within what timeframe. It should also include an explanation of the benefits of achieving these goals for the organisation and the individuals working within it. How, when and by whom the strategy is communicated can make a big difference to how it is received. For each group of individuals who are expected to contribute to the delivery of the strategy consider:

    - The best person (or persons) to communicate the 3Rs strategy. This individual needs to be committed to the strategy and positive about the difference that its implementation will make.

    - The messaging. The strategy needs to be relevant and to have appreciable benefits for each group of individuals such that they feel it is worth the effort required to contribute to its delivery. Communication of these benefits should be tailored to specific groups, and everyone should understand what the strategy means for them and how they will be required to contribute, including what support is available to help them. Getting the input of a communication expert to help with the messaging can be useful.

    - Addressing any concerns. The communication of the strategy is likely to give rise to questions. It can be helpful to think about this in advance and prepare FAQs for different groups.

Implementation plan

17. The 3Rs strategy requires a detailed implementation plan in place to ensure effective delivery and sustainability. The plan operationalises the strategy and should address the following points:

    - The assignment of accountability and responsibility for each specific objective in the strategy.
    - The resources required.
    - The timelines for specific objectives and priorities and the checkpoints for reviewing progress.
    - A list of risks and barriers that may influence delivery and how these will be mitigated.
    - Measures of success and how they will be collected and reported.
    - Changes that will be required in policies and practices as objectives are completed to ensure a sustained impact, for example, updating standard operating procedures or introducing new local training requirements. This avoids the risk that the impacts will be lost as it can be easy to revert to previous ways of working, particularly if a key individual moves on to another role or organisation.

18. It is important to ensure that the outputs and milestones that are delivered are communicated across the organisation and celebrated (e.g. at departmental events). This keeps the strategy in people's mind and will help future engagement as you move on to more ambitious objectives. The strategy should be a 'living document' that is reviewed regularly to ensure that it takes account of any organisational changes or scientific developments.

Resources required

19. It is possible to develop and implement a basic 3Rs strategy with no dedicated budget. However, all approaches will require some resource for staff to have time to discuss, develop, and implement a 3Rs strategy. Allocation of resource, whether that be funding and/or staff time, signals intent – a comprehensive 3Rs strategy that delivers coordinated, measurable and sustained changes will undoubtedly require new resource. The level required will depend on the priorities identified as part of the strategy and the actions required, the timeframe for addressing them and the existing level of commitment to the 3Rs. For example, funding may be required for events, prizes, research projects, new roles, recognising existing responsibilities, and/or infrastructure.

20. It is critical from the outset to have an awareness of the internal and external resources available for the delivery of a 3Rs strategy. It is important to note that it is possible to take action and make progress without waiting for all budget approvals to be in place, and in many cases securing a budget or additional resource can be easier once some examples of success have been achieved.

Indicators of success

21. The 3Rs strategy should be underpinned by indicators of success that allow progress to be easily tracked and reported. Metrics will vary depending on what your organisation is able to measure or record, how your strategy will be implemented, and the objectives and priorities that your 3Rs strategy defines. The 3Rs self-assessment tools provided by the NC3Rs (3rsselfassessment.nc3rs.org.uk) can help to track and benchmark progress, with one tool for evaluating on an institutional level, and one designed for use within individual research groups. In addition, the 3Rs evaluation framework published by the NC3Rs (nc3rs.org.uk/our-reports-and-reviews), while not specifically written for institutions, provides useful examples of quantitative and qualitative metrics that are helpful to consider.

22. Both institutional-level and objective-specific 3Rs metrics should be collated. Examples of institutional-level metrics include:

    - The number/proportion of research groups using the dedicated 3Rs self-assessment tool, provided by the NC3Rs, to collate, track and benchmark their 3Rs activities.
    - The number of departments (or research groups) with a nominated individual (a 3Rs champion) responsible for horizon scanning for 3Rs approaches relevant to the department's (or group's) work.
    - The number of 3Rs grants awarded to individuals (as lead researchers, and co-applicants) working within the organisation.
    - The number of individuals participating in activities (e.g. events or training) related to continuing professional development in the 3Rs.

23. Hypothetical case studies are provided below for each 'R' to illustrate the range of other types of metrics that can be collected depending on the specific objectives or priorities in the strategy.

Replacement example 1:

24. Institution A has six groups using mouse xenograft models for cancer research. Its 3Rs strategy includes an action to support researchers to adopt new approaches which replace the use of animals. The implementation plan includes tasking a small group of post-doctoral researchers to undertake a literature review to identify potential new approaches that may be relevant to their groups' needs. The review identifies a paper that has recently been published by a UK research team which describes a bank of well-characterised human organoid models that can be used for studying metastasis. The institution provides funding to allow two of the post-doctoral researchers to visit the UK team to learn how to culture the organoids in order to bring the technology in-house, and subsequently allocates funding for pilot studies to incentivise the relevant research groups to test the model in their own laboratories comparing utility to historical mouse data. Metrics of success include:

    - The post-doctoral researchers publish their literature review in an open access journal – the number of downloads and citations are recorded.
    - Three research groups are able to embed the organoids in their studies – information is already available on the groups' annual mouse use for xenograft studies (and the number of studies conducted) and this is used as a baseline to track how the introduction of the organoids changes their animal use over a five-year period.
    - The comparison of the organoid and animal data is published – the number of downloads and citations are recorded. The number of papers and amount of external funding secured using the organoid models is tracked over a five-year period.

Replacement example 2:

25. Institution B has included replacing the use of animal-derived materials as part of its long-term 3Rs strategy. As a first step a project group with staff from the purchasing and research governance departments as well as early career researchers is given responsibility for collating a list of the most commonly used animal-derived antibodies across departments. Three antibodies are identified as a priority for replacement and the project group is tasked with identifying commercial suppliers of the equivalent non-animal derived alternatives. The institution then allocates funding to enable comparative studies to validate the non-animal derived antibodies to be conducted by six research groups, helping to build an evidence base and confidence in shifting the use of reagents. In parallel, the purchasing department publishes a new section on the intranet highlighting commercial sources for non-animal derived antibodies and other research reagents and a new procurement policy is introduced in which written justification (reviewed by the animal ethics committee) is required prior to any order for an animal-derived product. In the longer term this approach is replicated for other animal-derived materials, such as cell culture components, with small amounts of funding provided for validation studies. Metrics of success include:

    - The number of animal-free products successfully identified as suitable replacements for animal-derived materials.
    - Generation of a preferred product/supplier list for antibodies and cell culture materials with validated alternatives.
    - The relative change in the use of animal-derived versus animal-free equivalent products tracked through purchasing over a five-year period.
    - The number of research groups adopting the use of the identified animal-free products.

Reduction example 1:

26. Institution C conducts a survey across its research community as part of the development of a 3Rs strategy to identify what actions would have the biggest impact on reducing animal use. Investment in small animal MRI is highlighted as a 3Rs priority area because of the opportunity to conduct longitudinal studies without the need for culling cohorts of mice at various timepoints. Based on this a number of research groups within the institution collaborate to secure a strategic equipment grant (with matched funding from the institution) for an MRI machine, resourced with two technicians to provide a new imaging service. Metrics of success include:

    - The proportion of eligible research groups using the service – each user is asked to record over a three-year period how many mice are "saved" when compared to the previous timepoint culls. Using this information, the technicians keep a running total that is regularly updated so that anyone using the imaging service can see the impact the switch is having.
    - The number of publications arising from the imaging service (and associated downloads and citations) is recorded.

Reduction example 2:

27. Institution D has a large number of mouse colonies across multiple facilities. A primary objective of the 3Rs strategy is to improve breeding efficiency and reduce wastage. To implement this, the animal ethics committee commissions a report on the outputs, usage and wastage within each colony over a three-month period, based on information within digital records and a survey of breeding practices. Results are discussed within the committee and a variety of recommendations are actioned, including new mandatory training for all technical and research staff managing colonies, better coordination to improve the sharing of commonly used strains across research groups, and a new policy on archiving to prevent the long-term use of 'tick-over' colonies. Measures of success include:

    - Number of individuals undergoing training.
    - Annual tracking by the animal ethics committee of mouse use and wastage using digital records, with comparison with previous years.
    - Number of strains archived and groups using the service (rather than keeping strains 'on the shelf' or generating strains *de novo*).
    - Number of groups sharing commonly used strains rather than maintaining their own colonies.

Refinement example 1:

28. Institution E has a large mouse facility. Following consultation with technical staff, its 3Rs strategy includes an action to reduce levels of aggression among group-housed male mice and subsequent single housing of injured animals. The implementation plan involves establishing a project team to benchmark the prevalence of aggression against the strain-specific inter-laboratory data reported in the NC3Rs Mouse Aggression Study (doi.org/10.1038/s41598-019-51674-z), and to review local implementation of the recommendations to prevent and minimise aggressive behaviour. The facility manager and project team organise for the animal technicians to record centrally all incidents of aggression-related injury observed during daily health checks, and a meeting is held to review mouse supply, grouping and husbandry practices. Metrics of success include:

    - The number of animal technicians involved in the data collection.
    - Establishing and benchmarking the prevalence of aggression-related injury among mouse strains housed within the facility over a three-year period.
    - A reduction in aggression-related injury and single housing of mice following changes to facility practice to implement the NC3Rs recommendations for reducing aggression.
    - Presentation by the project team and members of the technical staff of their findings and the refinement success at the annual congress of the UK's Institute of Animal Technology.

Refinement example 2:

29. Institution F uses rats for various study types. Part of the 3Rs strategy includes an objective to improve rat welfare. A senior individual within the animal facility is tasked with undertaking a review of housing and husbandry practices and, through this and consultation with the facility's staff, rat tickling (which mimics natural play habits, nc3rs.org.uk/rat-tickling) is identified as a minimal resource option that would suit the institution. With the support of the local animal ethics committee, the first step in the implementation plan involves appointing an animal technician as a "rat tickling champion". The champion visits other facilities where rat tickling is already part of standard practice and is tasked with familiarising themselves with the underpinning scientific literature, online information and educational resources. The champion subsequently leads small hands-on workshops and one-to-one sessions for animal care staff and researchers working with rats to introduce tickling, ensuring that there is a good understanding of how to identify which rats would benefit most from tickling as well as signs that indicate a positive emotional response. All technical and scientific staff working with rats are required to complete the online rat tickling certification course from Purdue University (bit.ly/30L5BTT). A standard operating procedure for tickling is introduced across the animal facility, including embedding tickling in the training of new starters who will be working with rats. Metrics of success include:

    - The number of rats that are regularly tickled (minimum twice weekly) as a proportion of all of the rats used at the facility is recorded and reported to the animal ethics committee annually.
    - The number of research groups routinely using rat tickling as part of their work.
    - The number of researchers and technicians who have completed the online rat tickling certification course from Purdue University.
    - A case study of the introduction of rat tickling is published on the Institution's website as part of its commitment to the 3Rs and openness. The number of visits is tracked.

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