



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

Choosing contractors for animal research outside of the UK

**NC3Rs guidance for researchers seeking funding
from UK public funders**

About this resource

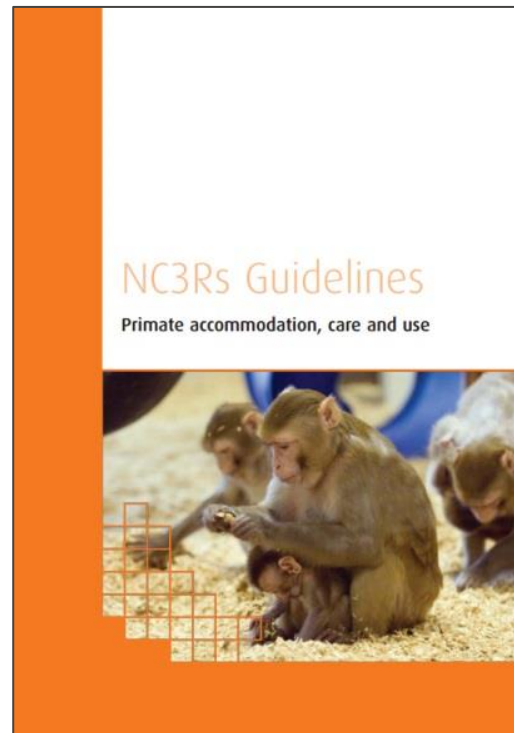
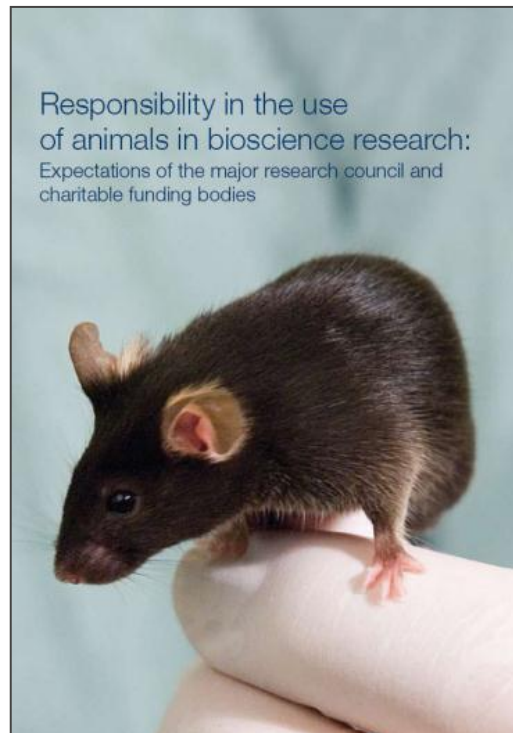
- This resource is primarily for those contracting work using animals for drug development studies.
- The principles also apply to any work conducted overseas as part of a collaboration.
- This resources covers:
 - [Funder policies and expectations.](#)
 - [Standards of animal housing and husbandry, with examples for dogs and macaques.](#)
 - [Links to useful resources for applicants.](#)
 - [Recommended actions for applicants.](#)

Funder policies and expectations

UK funder expectations on standards in animal research

UK funders expect high standards in animal research regardless of geographical location.

This includes meeting or exceeding UK standards of **animal welfare** and ensuring appropriate **experimental design** for preclinical studies at contract research organisations (CROs).



How these expectations are implemented

- Funders have adopted guidelines of good practice, compliance with which are a condition of research funding:
 - [Responsibility in the Use of Animals in Bioscience Research](#)
 - [NC3Rs Guidelines: Primate Accommodation, Care and Use](#)
- Research applications proposing the use of non-human primates, cats, dogs, equines and, in some cases pigs, are reviewed by the NC3Rs. For more information on the NC3Rs peer and advice service see: www.nc3rs.org.uk/peer-review-and-advice-service
- Specific requirements may be included in the terms and conditions of awards.

Applicants are responsible for meeting funder expectations

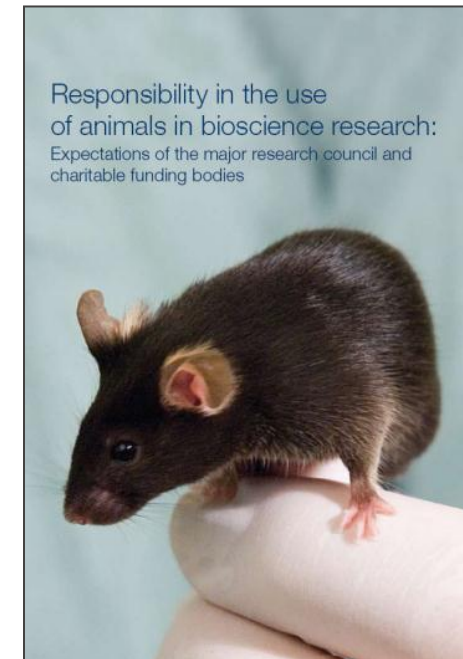
- Where applicants are using contractors to carry out their studies, compliance with the required standards is the responsibility of the applicant and this should inform the choice of contractor.
- Compliance against the required standards may be assessed by the NC3Rs on behalf of the funder.
 - Insufficient information on housing, husbandry and experimental procedures will cause delays in the application process.
 - Insufficient information on how the 3Rs will be implemented can lead to the application being declined or to delays in receiving funding.

The guidelines adopted by funders state that standards of animal research should be equivalent to those expected in the UK

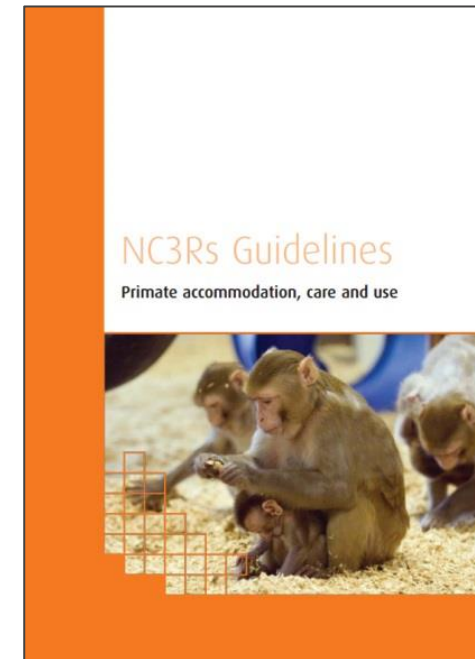
Applicants should familiarise themselves with these guidelines^{1,2} to:

- Understand the expectations of the funders.
- Understand the responsibilities of all parties involved in animal research.
- Submit a high quality application.

Additional resources to support applicants in meeting the expectations of funders can be found on the NC3Rs website: www.nc3rs.org.uk/peer-review-and-advice-service



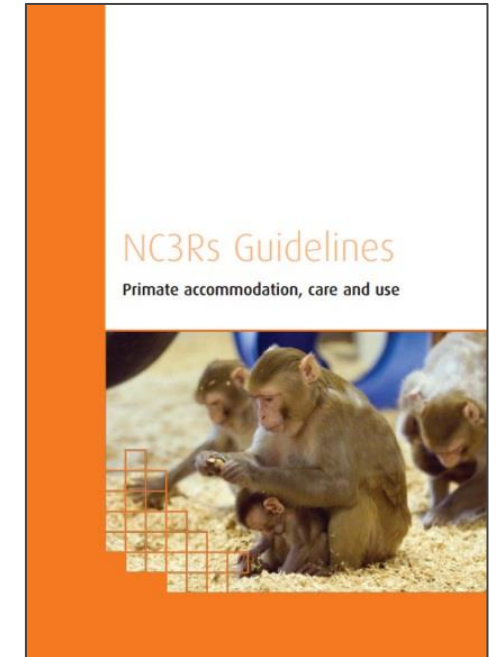
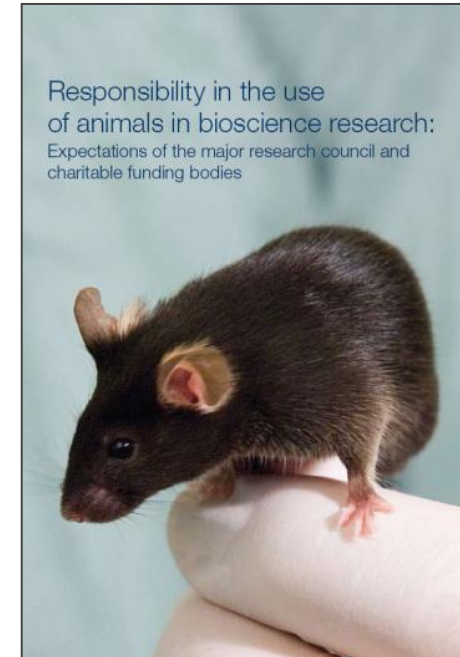
¹ For any species: [Responsibility in the Use of Animals in Bioscience Research](#)



² For non-human primates: [NC3Rs Guidelines: Primate Accommodation, Care and Use](#)

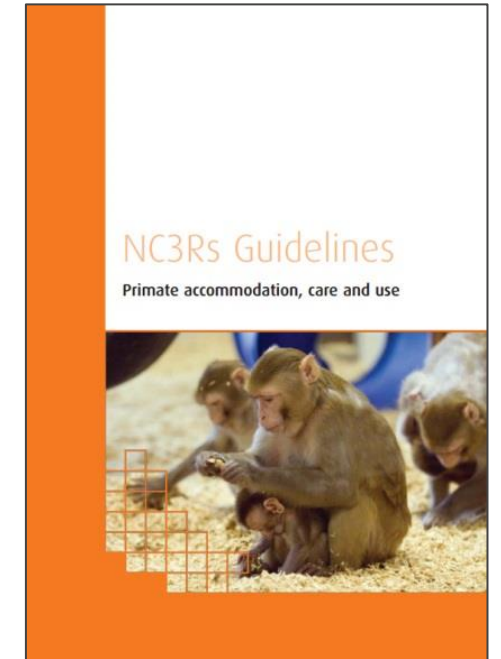
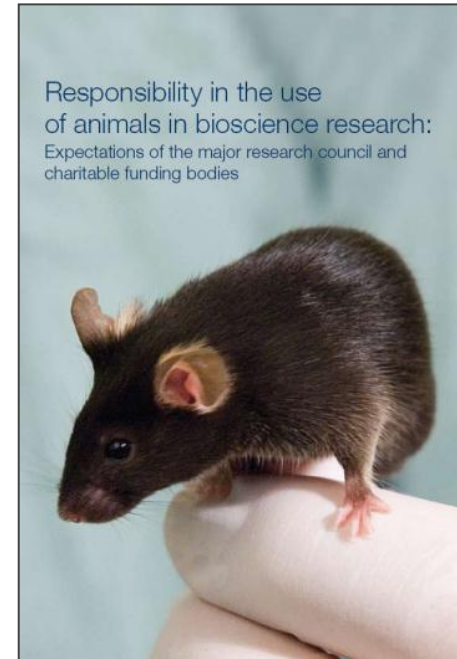
Key principles of the guidelines

- Apply the 3Rs to the experimental design and overall conduct of research involving animals.
 - For further information on the 3Rs visit: www.nc3rs.org.uk/who-we-are/3rs
- Meet (or exceed) the animal welfare standards provided under UK legislation regardless of geographical location.
 - [Code of practice for the housing and care of animals bred, supplied or used for scientific purposes](#)
 - [Animals \(Scientific Procedures\) Act 1986](#)



Conducting animal research outside of the UK

- Complying with local regulations is not sufficient unless these standards meet or exceed those in the UK (e.g. following the ILAR guide or having AAALAC accreditation is not sufficient).
- Applicants and their local ethics committee should ensure that collaborators and contractors apply standards consistent with the principles of UK guidance and legislation.



Space allocation

- Enclosure sizes and space allocations should meet or exceed those in the UK Home Office [Code of practice for the housing and care of animals bred, supplied or used for scientific purposes](#).
- In the case of dogs and macaques this can mean minimum space allocations of 5 to 12 times larger than those in the [ILAR Guide](#), depending on the specific circumstances.
- Where there are differences between local and UK guidance/legislation, whichever provides animals with the largest enclosure sizes and space allocations should be followed.
- Note that the expectations go beyond enclosure space. All animals should be provided with a complex and varied physical environment and social species should be housed in appropriate groups.

Standards of animal housing and husbandry, with examples for dogs and macaques

UK/EU space allocations for dogs compared with the ILAR guide

Location	Weight (kg)	Total floor area (m ²)	Minimum floor area for one or two dogs (m ²)	For each additional animal add a minimum of (m ²)	Height (m)
UK	< 10	4.5*	4.5*	2.0	2.0
UK	10-20	4.5*	4.5*	2.5	2.0
UK	> 20	8.0*	8.0*	4.0	2.0
EU	≤ 20	4.0*	4.0*	2.0	2.0
EU	> 20	8.0*	8.0*	4.0	2.0
US	< 15	-	0.74	-	†
US	≤ 30	-	1.20	-	†
US	> 30	-	≥ 2.40	-	†

* Dogs that are pair or group housed may each be constrained to half the total space provided (2.25 m² for a dog under 20 kg, 4 m² for a dog over 20 kg) while they are undergoing procedures, if this separation is essential for scientific purposes. The period for which a dog is so constrained shall not exceed four hours at a time. Dogs shall where possible be provided with outside runs.

† Cage height should be sufficient for the animals to comfortably stand erect with their feet on the floor. Enclosures that allow greater freedom of movement and unrestricted height (i.e. pens, runs, or kennels) are preferable.

US space allocations adapted from the ILAR guide.

UK/EU space allocations for macaques compared with the ILAR guide

Location	Weight (kg)	Age	Enclosure size (m ²)	Enclosure volume (m ²)	Volume per animal (m ³)	Height (m)
UK	-	< 3 years	2.00*	3.60*	1.00*	1.80*
UK	-	> 3 years	2.00†	3.60†	1.80†	1.80†
EU	-	< 3 years	2.00*	3.60*	1.00*	1.80*
EU	-	> 3 years	2.00†	3.60†	1.80†	1.80†
US	≤ 1.5	-	-	-	0.15	0.76
US	1.6-3.0	-	-	-	0.21	0.76
US	3.1-10.0	-	-	-	0.30	0.76
US	10.1-5.0	-	-	-	0.43	0.81
US	15.1-20.0	-	-	-	0.67	0.91

* An enclosure of minimum dimensions may hold up to three animals.

† An enclosure of minimum dimensions may hold up to two animals.

US enclosure sizes outlined in ILAR guide apply to any monkey species housed in pairs or groups.

Standard expectations for animal housing and husbandry

- Social species are housed in compatible pairs or groups.
- Solid flooring is provided.
- Animals are well habituated to humans and handling.
- Positive reinforcement is used to train animals for voluntary cooperation with scientific and husbandry procedures.
- Mice are picked up using [refined handling methods](#).

Any deviations from the above require strong scientific justification.

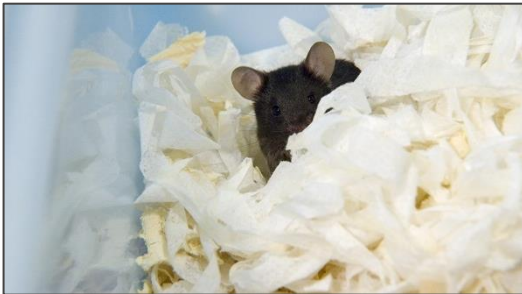


Environmental enrichment

Environmental enrichment should be provided to facilitate appropriate species typical behaviours and create a comfortable and suitably stimulating environment.

Examples of important species typical behaviours include:

- Nesting (e.g. rodents)
- Rooting (e.g. pigs)
- Climbing opportunities and access to sufficient vertical space (e.g. non-human primates)



Dog housing (1/2)

- Dogs should receive at least 20 minutes per day socialisation, exercise and olfactory stimulation outside of the home enclosure (e.g. in a designated enriched space).
- Environmental enrichment in the home cage does not substitute for out-of-pen exercise and socialisation.



Above: Examples of good practice.

Dog housing (2/2): unacceptable conditions

- Cramped metal cages with grid floors should not be used.
- Single housing requires exceptional justification and should be kept to a minimum time. Social housing should be the standard practice.
 - Most safety assessment studies can be completed with pair or group-housed dogs.
 - If separation is required for aspects of a study (e.g. feeding) this can be temporary (no longer than four hours).
 - For cardiovascular studies, telemetered dogs can be housed with naïve companions, or newer systems that transmit data on different frequencies can be employed.



Above: Examples of poor practice.

Macaque housing (1/4)

This image shows an example of a gang housing system at a UK facility for macaques on a toxicology study. Important features of the housing are:

- Sufficient space and complexity to permit a range of natural, species-specific behaviours and social housing in stable groups.
- Floor-to-ceiling height with elevated verandas for resting above human eye level.

Macaques are less aggressive and more cooperative when housed in cages with these features.



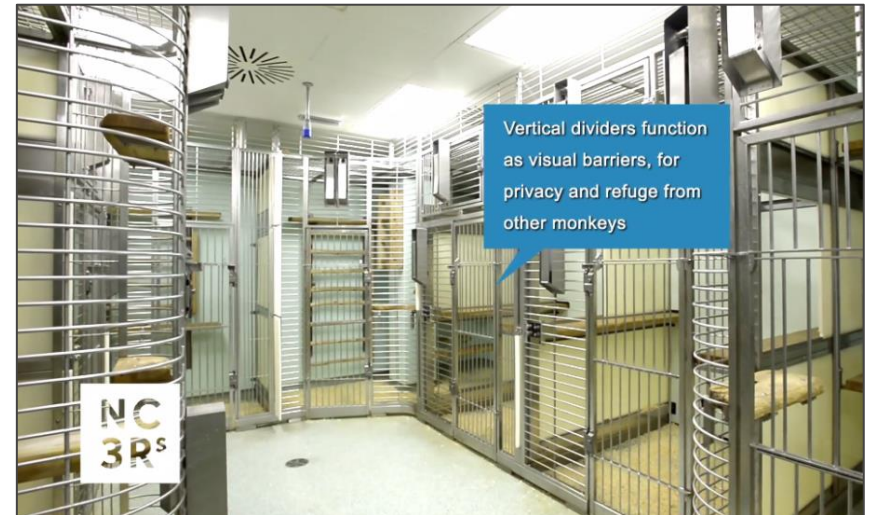
*Above: Macaques should have access to a **minimum** of 180cm of vertical space, or 200cm for breeding animals.*

Macaque housing (2/4)

Floors should be solid and covered with substrate such as wood shavings into which fine food items can be scattered, to promote natural foraging behaviour.

For further information on best practice for indoor caging of macaques visit:

www.macaques.nc3rs.org.uk/captive-management/housing



Macaque housing (3/4)

It is the applicant's responsibility to identify a CRO that can provide a standard of housing and husbandry compliant with funder expectations. This may require working with the CRO to ensure that adjustments to the housing are made, such as:

- Combining a bank of adjacent cage units to increase space.
- Linking the bank of caging to an additional enriched space to increase opportunities for exercise and social interaction (monkeys should have unlimited access to this area).
- Providing additional structural enrichment (e.g. verandas, panels, perches, swings).
- Converting the grid floor to a solid one and using floor substrate for foraging.
- Providing destructible materials, such as wood and cardboard.

Macaque housing (4/4): unacceptable conditions

- Cramped metal cages with grid floors should not be used.
- Single housing requires exceptional justification and should be kept to a minimum time. Social housing should be standard.
 - Toxicology and safety studies are routinely conducted with socially-housed macaques in the EU and elsewhere.
 - See the following slide for more information on socially housing monkeys under different research conditions.



Above: An example of unacceptable housing conditions.

Social housing of monkeys is achievable in the majority of circumstances




You can socially house monkeys...	Notes on how to achieve this
Under containment	Containment does not require individual housing. To avoid cross infection, animals in each group should receive the same treatment; staff safety can still be maintained.
With cranial or other implants	Following temporary separation (one day) post-surgery, monkeys can be successfully socially-housed for many years without damage to devices.
On telemetry studies	Modern systems transmit on different frequencies to permit social housing; use of naïve companion; Latin square designs.
Where individual food/fluid intake is measured	These measures are not routinely needed for most studies and observation of feeding/drinking habits or body weight can suffice; use cage/paired data; or commercial equipment (e.g. BioDAQ).
Where clinical signs are measured	It is often easier to detect clinical signs in a social group due to a richer behavioural repertoire; observing a group is more time effective.
Where urine is collected	Take a spot/catch sample; train monkeys to urinate on demand; customise housing; use cage/paired data.
When they are adults/may fight	Establish pairs/groups early; use behavioural data for partner selection; avoid disrupting social groups, but where this is necessary, introduce monkeys gradually under supervision; provide an enriched environment; monitor compatibility.
During feeding	Train for cooperative feeding where there is food aggression; account for resource guarding by providing sufficient food in a variety of ways (e.g. scatter feed and use enrichment devices).
During quarantine	In the event of individual clinical or subclinical disease it is common to treat nearest neighbours or the entire room.

Links to useful resources for applicants

NC3Rs resources for applicants

- [Search the NC3Rs resource library](#) for guidance and recommendations that could be applied to your project, such as:

- [Toxicology and regulatory science](#)
- [In vivo techniques](#)
- [Experimental design and reporting](#)
- [The Macaque website:](#)
 - www.macaques.nc3rs.org.uk
- [Dog housing and husbandry:](#)
 - www.nc3rs.org.uk/housing-and-husbandry-dog

<p>NC 3R^s National Centre for the Replacement, Refinement & Reduction of Animals in Research</p> <p>c.B.G.M.E.B. MEDICAL EVALUATION BOARD</p> <p>Re-evaluating the need for mAb chronic toxicity studies</p> <p>Key results and recommendations from an EPAA/MEB/NC3Rs collaboration focused on chronic toxicity studies for monoclonal antibodies (mAbs).</p> <p>WEBINAR AND VIDEO</p>	 <p>Minimising non-human primate use in drug development</p> <p>Opportunities to reduce the use of non-human primates in toxicology programmes.</p> <p>GUIDANCE</p>	 <p>Safety pharmacology</p> <p>Guidance on reducing or refining animal use for studies with cardiovascular, central nervous system and respiratory functional measurements.</p> <p>GUIDANCE</p>	 <p>Study designs for pharmaceutical and chemical development</p> <p>Projects providing guidance to reduce animal use or refine procedures within toxicology studies.</p> <p>GUIDANCE</p>
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Reducing animal use in preclinical studies

- Applicants are responsible for designing studies that use the minimum number of animals necessary to achieve the scientific aims.
- There are opportunities to apply the 3Rs in safety assessment studies without compromising drug development, including:
 - [Using a single species for longer term toxicity studies.](#)
 - [Reducing the use of recovery animals.](#)
 - [Minimising non-human primate use in drug development.](#)

www.nc3rs.org.uk/minimising-NHP-use

GUIDANCE

Minimising non-human primate use in drug development

Opportunities to reduce the use of non-human primates in toxicology programmes.

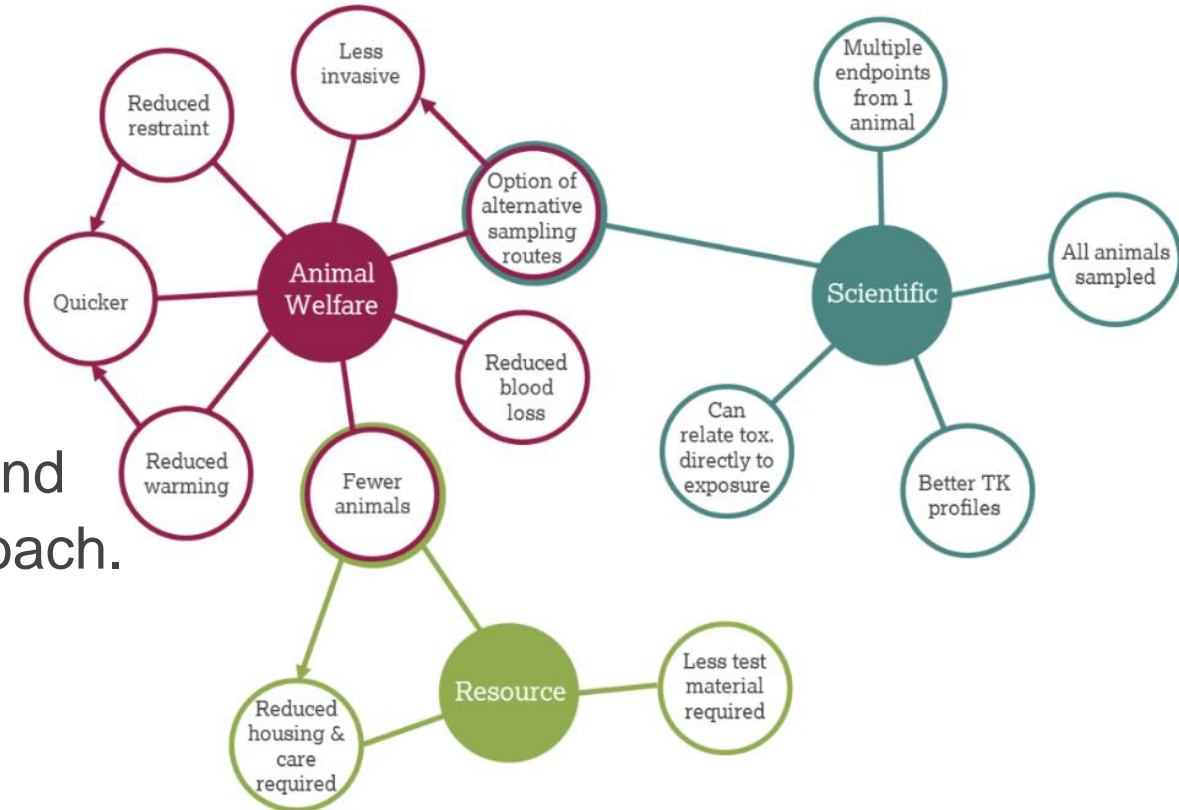
On this page

- Introduction
- Reducing animal use in mAb development
- Use of two species in regulatory toxicology studies
- Reducing the use of recovery animals
- Practical example of NHP reduction with a minimal study design
- Further reading

Reducing animal use and refining procedures in research and safety studies with blood microsampling

- Advances in bioanalytical techniques now allow smaller sample volumes (microsamples) to assess drug and chemical exposure in blood, plasma and/or serum.
- There are numerous 3Rs benefits associated with switching from traditional blood sampling methods to using microsampling techniques.
- Applicants should actively explore whether microsampling can be applied to their project and choose contractors that can facilitate this approach.

- www.nc3rs.org.uk/microsampling



Recommended actions for applicants

Applicants are responsible for obtaining the information required to assess compliance with UK guidance and legislation (1/2)

- **Ask questions**

- Speak to the scientists and veterinarians/animal welfare officers who will oversee your research at the CRO.
- Animal care and research staff are more likely to have the required information than the marketing/business development team.
- Use the questions in the funder's application form to guide your discussion.

- **Check understanding and feasibility**

- Ensure that the potential contractor understands and can deliver what is required, especially if there are language differences.
- Where improvements are necessary to meet the standards expected consider whether they have the appropriate knowledge and skills to deliver these.

Applicants are responsible for obtaining the information required to assess compliance with UK guidance and legislation (2/2)

- **See for yourself**
 - Request up-to-date photos of the enclosures and areas that will be used for the animals on your study.
 - Where possible visit the animal facilities before the work is placed, and during the study – this is the most robust way of ensuring the funders' requirements can be met.
- Note that, as the funders expect animal welfare standards consistent with those provided in the UK, UK and EU CROs are the most likely to be able to meet the required standards due to the regulations in place.

Before submitting your application, check whether you have:

- Read and applied the relevant guidelines adopted by the funding bodies as a condition of research funding (i.e. [Responsibility in the Use of Animals in Bioscience Research](#); [Non-human Primate Accommodation, Care and Use](#)).
- Obtained sufficient information to be confident that any contract research organisations meet the requirements of the funding body.
- Checked that the animal welfare standards will be equivalent to those provided in the UK and that you are able to provide a scientifically-principled justification for any exceptions.
- Ensured that you, or the CRO on your behalf, are implementing any relevant recommendations from [NC3Rs collaborative projects with the pharmaceutical industry](#).
- Provided clear and sufficiently detailed answers to all the animal use questions in the funder's application form.