Home Office

Guidance

Notes for Project Licence Applications

February 2024

Version 2

Contents

Introduction

These guidance notes are intended to assist project licence applicants, Named People and AWERB members on the process of preparing an application for a new project licence or amendment. They are specifically aimed at applications for the following purposes:

(a) Basic research

(b) Translational or applied research with one of the following aims:

(i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants

(ii) Assessment, detection, regulation, or modification of physiological conditions in man, animals, or plants

(c) Development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the following aims mentioned in paragraph (b)*

* Excluding any project that uses standardised protocol frameworks to produce data for submission to a regulator. ‘Standardised protocol frameworks' refers to published guidelines e.g., OECD, ICH. ‘Data’ refers to information produced in accordance with published guidelines and used by the licensee or others, as part of the submission to regulatory authorities.

Introductory details

Introductory details

What's the title of this project?

Focus on your broad aims and use simple language. For example, 'Genes and lifestyle influences on brain ageing'.

Title: Describe the theme and define the area of interest in a way that is likely to remain valid for the duration of the licence using lay language.

Licence holder

First and Last Name

Is this project for higher education and training purposes?

No

Which permissible purposes apply to this project?

- (a) Basic research
- (b) Translational or applied research with one of the following aims:
- (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants
- (ii) Assessment, detection, regulation, or modification of physiological conditions in man, animals, or plants
- (c) Development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the following aims mentioned in paragraph (b)*

Project licence duration

5 Years 0 Months

Which types of animals will be used in this project?

Examples:

- Mice

* Excluding any project that uses standardised protocol frameworks to produce data for submission to a regulator. 'Standardised protocol frameworks' refers to published guidelines e.g., OECD, ICH. 'Data' refers to information produced in accordance with published guidelines and used by the licensee or others, as part of the submission to regulatory authorities.

- Rats
- Beagles
- Domestic dogs (other dogs)
- Horses
- Rhesus macaques

Non-technical summary

All sections that form part of the non-technical summary (NTS) are identified by a yellow banner. These sections MUST NOT include any identifying features and must be written in lay language.

Creating your non-technical summary

Any information you enter on this screen will form part of a non-technical summary (NTS) that will be made publicly available. For this reason you should use everyday language that can be easily understood by members of the public.

You should also take care not to include information that could identify any people, locations, or intellectual property related to your project. You will be able to review and edit your NTS as a whole before you send your licence application to the Home Office.

Aims

What's the aim of this project?

Keep this to a short one or two sentence summary.

Example: To assess the efficacy of gene therapy to treat a range of lung and other human diseases.

Example: To determine whether combinations of drugs that inhibit a naturally occurring promotor of blood vessel formation (vascular endothelial growth factor [VEGF]) and chemotherapy are more effective than chemotherapy alone in preventing tumour blood vessel formation and growth.

Example: Identification of changes in nerve cells (neurons) that affect their excitability and are associated with the development of pain or numbness in peripheral parts of the body (e.g., hands and feet).

Why is it important to undertake this work?

Describe the value of this work as it relates to the permissible purpose and benefits. For example, you should include the significance of the knowledge gap (basic research) or impact of the clinical condition (translational research) that the project aims to address. Overall, you should present a rationale for using animals to obtain the expected benefits of the project.

Key words that describe this project

Choose up to 5. For example: cancer, stem cells, therapy.

Examples:

- Cancer
- Stem cells
- Cell signalling

Benefits

What outputs do you think you will see at the end of this project?

Outputs can include new information, publications, or products.

Outputs might be data, new knowledge in specified scientific areas, animals for use by others, vaccines, medicines etc and should reflect the stated permissible purpose(s).

Examples of benefits include publications and presentations, patents filed, candidate compounds expected to be progressed to clinical trials, approaches to therapy expected to be discontinued, animal welfare gains, or influence on public policy.

The benefits need to be realistic, achievable in the duration of the licence and specific to this project. You can briefly outline potential future additional benefits this work may lead to, but it should be clear what you expect this project to achieve, as opposed to claims based on future work that is not part of this application.

Discovery research that advances knowledge in a particular field is acceptable as a benefit. Outlining the potential for translation is useful, but not essential and such explanations should be brief.

Who or what will benefit from these outputs, and how?

The impact of these outputs may be seen in the short-term, or they may not be fully realised until you've completed the project. Consider all timescales in your answer.

Examples include the research group, others at the establishment, other researchers, the pharmaceutical industry, clinicians, patients, or animal welfare.

Will this work be offered as a service to others?

No (This Guidance does not cover service licences).

How will you look to maximise the outputs of this work?

For example, collaboration, dissemination of new knowledge, or publication of unsuccessful approaches.

Further examples include publication in open-access journals, presentation at scientific meetings, making resources available to other researchers (e.g., data, animals, tissues).

Project harms

Explain why you are using these types of animals and your choice of life stages.

Provide a scientific justification for all chosen species and their life stages.

Typically, what will be done to an animal used in your project?

For example, injections and surgical procedures. Include any relevant information about the duration of experiments and the number of procedures.

Provide a comprehensive description of the procedures that animals will undergo. Include 'standard' techniques such as injections, imaging, general anaesthesia etc. This might include:

- how the animals are kept e.g., accommodation, food, and water.
- substances administered including route(s) and any restraint.
- a description of surgical procedures.

Example: During surgical procedures, we will typically make very small windows in the skull to gain access to the brain, implant tiny screws and probes no more than 4 mm long, then secure everything with dental cement before closing the wound. These surgeries will typically last 2 hours.

Example: Typically, animals will experience brief, slight discomfort and no lasting harm from administration of substances by injection using standard routes (intravenous, subcutaneous, intraperitoneal). Where administration is required for prolonged periods, animals will be surgically implanted with slow-release devices such as a mini-pump. These animals will experience some discomfort after surgery that may result in reduced activity or appetite and will be treated with analgesics. Animals will undergo changes in diet which are not expected to cause distress but may sometimes result in obesity or itchy skin. Some diets may result in weight loss due to unpalatability. Animals will be placed onto normal diet should they lose 20% of their body weight. Animals will experience very brief discomfort from blood sampling associated with insertion of a small needle through the skin. The final procedures will be undertaken under non-recovery anaesthesia where the animals will only be aware of the anaesthetic being administered and may briefly experience distress and no pain.

What are the expected impacts and/or adverse effects for the animals during your project?

Examples can include pain, weight loss, tumours, or abnormal behaviour. State the estimated duration of these effects on an animal.

The adverse effects should be described in terms of what the animal is likely to experience. All the harms caused to the animals should be covered. If animals may die as a result of procedures this must be described.

A lay reader should be able to understand the degree and duration of harms and be clear what the greatest level of severity expected and the proportion of animals likely to experience this level of suffering. Unqualified general terms such as 'moderate' are not helpful.

Example: Mice will have minor surgery to implant a device under the skin that can release a medicine slowly. They are expected to recover quickly and will be given painkillers and post-operative care just like people recovering in hospital.

What are the expected severities and the proportion of animals in each category (per animal type)?

The expected severities should reflect the prospective severities of the protocols. However, the expected severities may include non-recovery, sub-threshold, mild, moderate, and severe. Further information regarding the severity classification of procedures can be found in Appendix G of the Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 (Guidance on the operation of the Animals (Scientific Procedures) Act 1986 - GOV.UK (www.gov.uk)).

Example: Mice: 75% mild, 25% moderate and Rats 50% mild, 50% moderate.

Example: Breeding and maintenance of GA Mice 10% mild and 90% sub-threshold.

Fate of animals

What will happen to animals at the end of this project?

- Killed
- Kept alive
- Set free
- Rehomed
- Used in other projects

Further information regarding the fate of animals is available in the Home Office Advice Notes on Use, Keeping Alive and Reuse (Advice Note: Use, keeping alive and re-use) and Rehoming and Setting Free (Advice Note: Rehoming and setting free

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Replacement

Why do you need to use animals to achieve the aim of your project?

Provide a scientific justification for and evidence to support the use of animals in your project. Demonstrate that you have considered existing data to avoid unnecessary duplication and whether the scientific question can be answered by existing animal or in vitro studies.

You should demonstrate that the project does not include unnecessary duplication, includes evidence-based choices of animal models and that a structured review of alternatives has been conducted. You may describe the use of resources such as SyRF, a free online platform for researchers to perform a systematic review and meta-analysis of animal studies. The platform was developed by CAMARADES and group funded by NC3RS: SyRF: the CAMARADES/NC3Rs in vivo systematic review and meta-analysis facility | NC3Rs

Explain if you will be able to replace any part or all of your proposed animal use during the course of this programme of work.

Example: We need to use animal models to understand how antibodies are generated in response to vaccination. This process happens in lymphoid tissue that are very complex structures with many different cell types interacting and communicating with each other. In addition, these immune cells are in constant movement that allows them to interact with different partners at different stages of their development. These processes are so complex that currently no in vitro system is able to replicate this. Current alternatives include ex vivo tissue culture, microfluidic devices, and engineered tissues. Ex vivo tissue culture using human tissues are limited by the isolation of the lymphoid tissues from blood and lymph flow. Although microfluidic devices can model certain elements of the lymph node immune response, they cannot currently reproduce the immune function of the organ. While engineered tissues offer opportunities to study elements of lymph node function, they currently are unable to replicate the structure of the organ.

Which non-animal alternatives did you consider for use in this project?

You must demonstrate that you have considered all possible alternatives for your programme of work by describing the steps you have taken to actively research non-animal alternatives. Your AWERB and Named Information Officer (NIO) can help you find suitable databases and websites (e.g., EURL ECVAM publications, the Norecopa 3R Guide database). You should specifically describe the literature and databases that you have utilised and the search methods and terminology that you have employed. You should include details of any relevant research that indicates all or some of the models you wish to use could be replaced. For example, have you fully considered practicable alternative approaches such as:

- computer modelling;
- in vitro methods such as cell culture, organs on a chip, organoids, phage display anti-body production;
- non-protected species such as fruit flies or nematodes;

- human or epidemiological data.

Why were they not suitable?

In some cases, replacement methods may be able to answer some of your scientific questions and you can describe any limitations here. Where relevant research indicates all or some of the models you wish to use could be replaced you must explain why your research is an exception.

Reduction

Enter the estimated number of animals of each type used in this project.

Mice: Number **Rats:** Number **Beagles:** Number **Horses:** Number **Rhesus macaques:** Number

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How have you estimated the numbers of animals you will use?

Do not mention POWER calculations here. If relevant, there will be an opportunity to provide these details elsewhere.

Where appropriate, outline the principles of experimental design you will use at each stage of the work, indicating:

- how the different experimental groups (controls, dose levels, satellites etc) will be chosen;
- how control groups are used. Provide a robust scientific justification for the use of sham surgical controls;
- how you will maximise the data output from the animals you use;
- how likely variability will be determined and minimised;
- how group sizes will be set. Does data exist from previous work?
- how studies are randomised and blinded;
- when and how pilot studies will be used;
- how comparisons will be made between groups or experimental situations;
- how data are analysed to ensure the maximum efficiency of animal use.

The experimental principles should achieve reliable results, avoid unnecessarily repeating experiments, and allow decision making. Considerations are not simply about using few animals; sufficient animals need to be used to achieve the stated objectives. An inadequate group size in experiments leading to unsatisfactory results is a waste of animals. Small groups will suffice for pilot studies. See: https://www.nc3rs.org.uk/3rs-resources/conducting-pilot-study

Example: A statistician helped us with calculations using typical variations from our own earlier experimentation to calculate minimum numbers of animals to be used whilst ensuring that the results are statistically significant. Sample sizes for our experiments are estimated from past experiments. Calculations typically show that we need group sizes of 8 to achieve the quality of results we need. We've used our annual return of procedures data to estimate the number of animals that we will need to use for breeding.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?

You may want to reference online tools (such as the NC3R's Experimental Design Assistant) or any relevant regulatory requirements.

Considerations:

- what measures have been or will be taken to minimise and control the sources of variability within your project and its component procedures?
- what experimental design principles will be followed and what sources of specialist advice will you consult? e.g., statistical support.

Example: We employed the NC3Rs' experimental design guidance and experimental design assistant (EDA) to plan our experimental design, practical steps and statistical analysis utilising the advice and support for randomisation and blinding, sample size calculations and appropriate statistical analysis methods. We will use the EDA diagram and report outputs to support experimental planning with animal users.

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

This may include efficient breeding, pilot studies, computer modelling, or sharing of tissue.

Consider what other measures have been, or will be, taken to maximise success and minimise unnecessary use of animals?

Include other measures that you will use to reduce the number of animals used such as use of ex vivo material from tissue banks or surplus stock.

Example: At the end of the experiment, we will harvest as many tissues as possible at post-mortem. If we don't need to analyse the tissues immediately, we will freeze them and make them available to other researchers working on similar questions.

Refinement

Which animal models and methods will you use during this project?

Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

Explain your choice of model(s) and method(s), showing, as relevant to your programme of work:

- why the model(s) and methods selected are together likely to result in the least pain, suffering distress or lasting harm to the animals involved to achieve the scientific benefit;
- what other options are available;
- what principles are followed when selecting between options of different severity;
- why further reductions in the intensity or duration of adverse effects cannot be achieved;
- how you will ensure that animals are maintained in the best physiological state;
- why it is not possible to conduct your studies using earlier end points.

Include specific justification for withholding any treatments or standard husbandry practices that may impact on animal welfare.

Include specific justification for any protocols that may be classified as severe.

Example: Some animals will be allowed to grow old to study the immune response in the ageing animal. To induce gene expression in animals or to deplete specific cells, some animals will be given substances by mouth, injection, or through food. Oral gavage or injection can be necessary to induce a rapid change in gene expression. This will let us to study processes that happen within short time periods of a few hours. We will have to induce immune responses to study the response to vaccination. Animals will be vaccinated using methods similar to human vaccination, e.g., injection of substances under the skin.

Why can’t you use animals that are less sentient?

For example, animals at a more immature life stage, species that are less sentient, or animals that have been terminally anaesthetised.

Explain why you cannot further reduce the capacity to suffer, for example using anaesthesia or using animals at a different life stage.

Example: Non-mammalian animals are limited in their use because they either do not have the right type of immune cell or their immune system is too different from the human immune system to provide relevant results. We can’t use embryos or very young animals as their immune system is immature and doesn’t respond to antigenic stimulation in the way mature animals do.

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?

Explain how you intend to refine the studies during the course of this project.

Example: We will regularly check information on NC3Rs website, we've signed up to the NC3Rs newsletter, we will meet the NC3Rs Regional Programme Manager, and attend Regional 3Rs symposia.

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?

Potential refinements include increased monitoring, post-operative care, pain management, and training of animals.

What strategies will you use to reduce severity to establish earlier endpoints at which you can gain satisfactory data? For example, a frequent monitoring regime (if necessary, throughout the night), use of score sheets, or use of biomarkers. You should consult published guidelines to ensure refinement of particular disease models, for example IMPROVE guidelines for stroke models: IMPROVE-ing animal welfare in experimental stroke research | NC3Rs

Example: Ageing animals will be carefully monitored by staff trained to work with ageing animals. Group sizes in ageing experiments will be increased to accommodate for loss of animals and to avoid single housing due to animal losses due to old age. Longer drinking spouts will be used, and animals will be monitored for adverse effects such as changes in weight, dermatitis, piloerection, paleness, changes in mobility, lumps, eye defects, abnormal respiration, or stools. If these are observed animals will be treated accordingly, and animals that develop severe effects will be humanely killed.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?

There are published guidelines to assist with planning animal research and testing, such as the PREPARE guidelines:
http://journals.sagepub.com/doi/full/10.1177/0023677217724823

Further information about the PREPARE guidelines can be found here:
https://norecopa.no/prepare

Other resources are available including guidance and publications from the NC3Rs and Laboratory Animal Science Association.

Applicant information

Experience

Have you managed similar work in this field before?

Yes/No

What were your, or your group's, main achievements that are relevant to this application?

Summarise how you have achieved benefits from previous projects or your current work.

Example: Under my current licence, I have published five papers in peer-reviewed scientific journals and expect to publish another five in the next twelve months. We have made several 3Rs gains including replacing an in vivo model with an in vitro one to cover around 20% of the programme.

What relevant scientific knowledge or education do you have?

Please look at the Guidance para 5.2 (page 39) 'Who can hold a project licence' and make sure you can comply with all the requirements.
https://www.gov.uk/government/publications/operation-of-aspa

Provide a brief overview of relevant scientific knowledge and specific knowledge relating to all the species of animal that will be used in the programme of work.

Example: I gained a BSc degree in farm animal science from the University of XXX in 2005 and a PhD in bovine nutrition in 2009. Subsequently I held the post of a post-doctoral research associate on a cross disciplinary project relating milk yield to nutrition in commercial farms. Resultant findings led to a BBSRC-funded grant, on which I was employed as a researcher co-investigator and was responsible for directing the work of a post-graduate researcher and planning the experiments for the group.

What experience do you have of using the types of animals and experimental models stated in this licence application?

Consider how long you have worked with research animals and with which species, how long you have held a UK project and/or personal licence, and how long you have carried out experiments on animals if not in the UK.

If you have held a project licence before and are now proposing to use a new species or include work falling under a different personal licence category than your previous work (e.g., your application now includes surgical procedures) then you must add details of how you have gained the relevant additional knowledge and experience required.

Example: Technical expertise acquired through 31 years relevant experience. I am personally experienced in all the procedures to be applied to all the species in this application with the exception of the diabetes model described in protocol 4. While I have limited experience of diabetes models, I will be mentored by Professor Black who has experience of this model and will be guided by the NACWO and NVS, particularly in matters relating to the 3Rs.

What experimental design and data analysis training have you had?

If you do not have this expertise, how will you access it?

Example: In May 2023, I attended a workshop at my establishment on experimental design run by our establishment statistician. I completed a course in biological statistics in 2020 as part of my MSc.

Why are you the most suitable person to manage this project?

Your role, seniority, or expertise in managing projects of this nature may be relevant.

Example: I recently started my independent academic career, obtaining a 5-year fellowship position funded by XXX. As the Principal Investigator on this grant, it is most appropriate for me to take responsibility for the research involving animals. I line-manage a team of one post-doc researcher, one PhD student and two laboratory technicians, hold the budget for the work and have gained sufficient experience and understanding of the role whilst working under Prof Brown, gradually increasing my project management responsibilities over the last three years.

Example: I am an established project licence holder having held three previous project licences to cover this ongoing programme of work.

What relevant expertise and staffing will be available to support you?

Include examples of practical or specialist support you'll be able to draw on. If anyone is going to help manage the project, explain how.

Example: The bovine nutrition group at XXX University consists of three PIs with a wide range of skills and expertise, and extensive experience in planning and performing in vivo studies. Surgery will be performed with the advice and guidance of Dr Pink, a large animal surgeon at XXX who has experience of this type of surgery and excellent success rates. The NVS has extensive experience in bovine anaesthesia. The dosing protocols will be optimised with the assistance of Prof Green and his group members, who have experience of using this method successfully.

Funding

How do you plan to fund your work?

If you do not have full funding, explain how you will stage your work and the likelihood of you obtaining further funding.

It is not essential that you have funding for the whole five years in place, but please indicate how long you expect your current funding to last. If you have no or little funding, explain your plans for funding the programme of work and comment on your track record of securing funding for this kind of work, where applicable. We need to be clear that funding is or is likely to be available. This is to provide reassurances that you won't run out of funding before benefits have been achieved, thereby wasting animals and causing unjustified suffering. This is particularly important for longer term studies, those resulting in severe severity or using special species.

Example: I have recently started my independent academic career, obtaining a 5-year fellowship position funded by XXX. This will fund the proposed work in full.

Example: The work outlined in protocols 1-3 is funded by a Career Development Fellowship from XXX and underwent rigorous peer review prior to funding. The work outlined in protocol 4 has been submitted as an XXX project grant. If funding for the work in protocol 4 is not secured, this work will not go ahead.

Will this work support basic or translational research, or non-regulatory drug or device development?

Yes (Purposes a, b, and c)

Were any grant applications for this work peer reviewed? If so, by whom and what was the outcome?

Basic or translational research, or non-regulatory drug or device development includes all projects for permissible purposes (a) and (b) and may include projects for purpose (c).

Independent peer review by a research council or equivalent will give confidence in the scientific quality of the proposal.

Example: Work to meet objectives 1 and 2 was peer reviewed by Research Council A and Charity B as part of my application for funding.

Training

Do you need to update this training record?

The training record must be complete listing the required modules and including either details of training certificates or grounds for exemption (e.g., project licence held within the last 5 years).

Project location

Establishments

Will your project use any additional establishments?

Yes/No

Additional establishment 1

Select an establishment where work will be carried out

Establishment 2

Why do you need to carry out work at this additional establishment?

For example, there may be important specialised equipment at this location that is not available at your primary establishment.

Information in this section contributes to the assessment of whether a successful outcome is likely and allows consideration of how the movement of animals between sites may contribute to the overall harms or affect the quality of the outcomes.

Who will be responsible for supervising your work at this additional establishment?

This should be someone who has appropriate expertise, training, and authority.

Do the housing, husbandry, and care conditions at each establishment meet the requirements laid out in the Code of Practice for each type of animal you will be using?

Please read the Code of Practice for the housing and care of animals bred, supplied, or used for scientific purposes before you answer.

Yes/No

If any establishment does not meet these requirements, or if any type of animal you're using is not listed in the Code of Practice, explain how you will ensure that housing, husbandry, and care conditions are appropriate for your project.

If there is a scientific reason, then an exemption will be needed from PEL SC4(7).

For example, there is no specific ASPA Code of Practice for animals such as wild boar, so we need a brief explanation of how appropriate conditions are provided.

Transfer and movement of animals

Will any animals undergoing regulated procedures be moved between licensed establishments?

This includes genetically altered animals being bred or maintained under the authority of your project licence.

Yes/No

What types of animals do you need to move? What regulated procedures will they have undergone?

Provide the type of animals and information on when in the series of regulated procedures, they would be moved.

We don't need details relating to acquisition of GA animals which have undergone only production and identification/genotyping as the reasons and potential harms are well known.

Why do you need to move animals between licensed establishments?

Describe the reason and justification for the movement of live animals.

How might the movement of animals between licensed establishments affect scientific delivery of the work?

Where movement may confound the scientific integrity of the experiment describe how this will be addressed including strategies for management and mitigation.

What measures will you use to minimise any adverse effects for animals that may arise when moving them between licensed establishments?

Example: The body weights and clinical signs of animals will be assessed 24 h before transport by a NACWO and/or NVS and only those animals gaining weight will be permitted to travel. Animals may have mild respiratory signs (e.g., mildly increased respiratory rate) but all other clinical and behavioural parameters will be normal. Prior to transport animals will be placed in their transport boxes with bedding from their home cages. Animals will be transported with their cage mates and provided with fluid (in the form of gel packs) and food. Animals will be transported in temperature controlled vans with same day delivery.

Will surgically prepared animals be given a minimum of 7 days to recover before being transferred?

Yes/No

Why won't animals be given 7 days to recover before being transferred?

Provide scientific justification where animals will not be permitted 7-days to recover from surgery prior to transportation.

Will animals be given a minimum of 7 days to acclimatise to their new surroundings prior to any regulated procedures being undertaken?

Yes/No

Why won't animals be given 7 days to acclimatise to their new surroundings?

Provide scientific justification where animals will not be permitted 7-days of acclimatisation to minimise transport stress effects.

Places other than a licensed establishment (POLEs)

Will any part of your project be carried out in any places other than a licensed establishment (POLEs)?

Yes/No

Why can't this part of your project take place at a licensed establishment?

You must provide a scientific reason why you need to work at a POLE. See also Advice Note ‘Working with animals taken from the wild’.

Explain why the procedures can’t/shouldn’t be done at a licensed establishment.

Explain what procedures will be done at the POLE (i.e., which protocols/procedures) and why they need to be done there.

Details about keeping animals alive and setting them free to the wild (if appropriate) should be included in the relevant sections.

Information about animals that are taken from the wild (or obtained from other non-establishment sources) and moved to an establishment before any regulated procedures are carried out should not be included in this section; instead, this should be included in the Plan of Work and Source of Animals sections. For details of the information required see section 3 of the Advice Note ‘Working with animals taken from the wild’.

POLE 1

Name

POLEs may include places such as inland waterways or farms. List POLEs either as specific locations, if known, or in more general terms. See Guidance para. 5.7.6 and Advice Note ‘Working with animals taken from the wild’.

Details

This section requires details of all regulated procedures done at places which are not included in an establishment licence, and not just those done to animals “in the wild”.

Note that if you are working with wild animals, you also need to provide information as prompted in the section 'Animals taken from the wild'.

POLEs may include places such as inland waterways or farms. List POLEs either as specific locations, if known, or in more general terms. See Guidance para. 5.7.6 and Advice Note ‘Working with animals taken from the wild’.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/660242/working-with-wild-animals-160706.pdf

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How will you ensure that procedures taking place at these POLEs can be inspected?

For example, how will you obtain consent from landowners?

Note that a condition will be placed on your licence requiring you to provide notification to ASRU a minimum of 7 days prior to work at a POLE.

How will work at each POLE be done in the most environmentally sensitive manner?

This may include information on how you will mitigate the potential impacts on the environment of the procedures taking place e.g., minimise disturbance to non-target species during trapping.

Will any animals be moved between a POLE and a licensed establishment during this project?

Yes/No

Why do you need to move animals between a POLE and a licensed establishment?

If you need to start regulated procedures on animals at a POLE and then move these animals to an establishment, you should explain:

- why you need to move them;
- how you will ensure that they will be in a suitable condition to travel;
- what arrangements will be made to assure their welfare during transport, particularly if they are being moved after the start of regulated procedures;
- any impact such movement will have on the scientific data to be collected

What arrangements have been made to ensure animals can be safely transported and that any permits necessary to transport the species under study are/will be held?

Provide relevant details.

How might the movement of animals between a POLE and a licensed establishment affect the scientific delivery of this project?

Provide relevant details.

How will you ensure that animals are in a suitable condition to be transported?

Include all checks that will be made for suitability and what will happen to animals that are not suitable to be transported.

Provide relevant details.

Who will be responsible for checking the animals before they are transported?

This does not need to be a Named Veterinary Surgeon.

Provide relevant details.

How will you ensure that this person is competent to make the appropriate checks?

Provide relevant details.

What arrangements will be made to assure an animal's welfare during transport, particularly if they are being moved after the start of regulated procedures?

Provide relevant details.

Project plan

Scientific background

Will this work support basic or translational research, or non-regulatory drug or device development?

Yes (Purposes a, b, and c)

Briefly summarise the current state of scientific knowledge in this area of work to show how you arrived at the starting point of this project.

Be specific and relevant to your project aim - there's no need for a detailed overview of the entire field. Include any relevant non-animal research if it has contributed to the starting point of your project.

The information in this section gives the inspector the background information they need to understand the context of the application within the relevant scientific field(s).

Briefly set out the current state of knowledge on which the current project intends to build. How have you come to the start of the (new) five-year project?

Ensure the background is specific and relevant to the aims and objectives of this project – the background section should not be a detailed overview of the field and relevant literature.

Include any relevant research not involving animals that contributes to the starting point for this project.

Present key arguments concisely.

Use references from your group and the work of others (and/or regulatory guidelines if appropriate) and outcomes of past work to support the main points stated and the models to be used.

Ensure specialist acronyms relevant to your science are defined the first time they are used.

Refer to progress made under any previous project (including outputs, benefits and 3Rs advancements) that are relevant to this application. For example:

- publications;
- GA strains to be used in further research;
- compounds advanced to development;
- therapeutic or scientific approaches discarded;
- products taken to clinical trials or approved;

- patents;
- contribution to policy initiatives.

What new knowledge do you hope to discover that will address a gap in fundamental scientific knowledge or meet a clinical need?

Refer to the basis for any scientific hypotheses you plan to test during this project.

Refer to hypotheses and expected benefits.

Does your project mainly involve translational or veterinary clinical applications?

Yes (Purpose b or c)/No (Purpose a)

How prevalent and severe are the relevant clinical conditions?

For a disease-specific biomedical discovery programme, briefly explain the prevalence and severity of the condition, availability of treatments and why a different therapeutic approach is necessary in the following sections.

Example: Around 5 million people in the UK have diabetes and this number is predicted to increase to 5.5 million by 2030. Around 90% of people with diabetes have type 2 diabetes and around 8% have type 1 diabetes. About 2% of people with diabetes have rarer types of diabetes (www.diabetes.co.uk/nhs/). Over time, diabetes can lead to damage to the heart, blood vessels, eyes, kidneys, and nerves. Adults with diabetes have a two- to three-fold increased risk of heart attacks and strokes, increased chance of foot ulcers, infections, and limb amputation. Moreover, diabetic retinopathy is an important cause of blindness responsible for 2-3% of global blindness. Diabetes is among the leading causes of kidney failure. Type 2 diabetes and its complications consumes approximately 10% of the NHS budget.

What are the problems with current treatments which mean that further work is necessary?

Example: There is currently no cure or type 1 or type 2 diabetes, and most therapies are based on insulin replacement (Type 1 diabetes) and/or the increase of glucose sensitivity by peripheral organs and/or the stimulation of insulin secretion by the beta cells (Type 2 diabetes). More recently, bariatric surgery, which was originally developed as a weight-loss intervention, has been found to improve various metabolic co-morbidities of obesity, particularly type 2 diabetes. Bariatric surgery induces long-lasting remission of hyperglycaemia and reduces cardiovascular disease and mortality associated with Type 2 diabetes. However, the mechanisms by which bariatric surgery asserts is beneficial effects are not well understood.

What is the scientific basis for your proposed approach?

Example: To understand how bariatric surgery exerts its beneficial effects, and thereby make improvements to treatment of diabetes. we will identify the genes that play key parts in glucose homeostasis and determine how they contribute to glucose regulation. as well as increase our understanding of how anti-diabetic treatments exert their beneficial effects.

Will you be producing data primarily for regulatory authorities that use standardised protocol frameworks?

Yes/No

Will you be undertaking non-regulatory testing or screening as a service to others?

Yes/No

Will you be producing genetically altered or surgically prepared animals/animal products using standardised protocol frameworks as a service to others?

This includes projects to create, breed, maintain and supply genetically altered animals to researchers within the establishment, projects taking blood and other tissues for researchers and other clients within and/or external to the establishment.

Yes/No

Will you be manufacturing vaccines and medicines for medical or veterinary use?

Yes/No

Do you need to transfer animals from a project that's due to expire?

Yes/No

Project licence number

PPL Number

Expiry date

For example, 13 06 2019

Enter correct expiry date of current licence.

Action plan

Objective 1

Objective title

Describe objectives to achieve the overall aim. You may wish to describe these objectives as questions (see examples below). Objectives should be realistically achievable based on available funding, staffing and other resources. You may not be able to identify all objectives at the time of application. Additional objectives can be added as amendments if they fit within the overall aim.

Usually, general terms like “cancer”, “nervous system”, “receptors” or “pathways” are too broad without specific explanation of what you are aiming to do e.g., Which types of cancer? What aspects of disease? What elements of the nervous system, with what effects?

Try to ensure your objectives reflect the outcomes you want to achieve, not the methods you will be using to achieve the outcomes. For example, creating a new line of genetically altered mice is a method of achieving a scientific objective rather than the scientific outcome desired.

Basic research example: Does mis-expression of candidate genes affect the stem cell compartment and/or alter tumour susceptibility in animals? How would anti-cancer drugs alter the Myc and other (p53/Ras) oncogenic systems?

Objective 2

Objective title

Translational research example: Determine the pathogenesis of the infectious organisms in pregnant and neonatal pigs

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How do each of these objectives relate to each other and help you to achieve your aim?

Outline any interdependencies, stop: go points, and milestones. Include any key in vitro, ex vivo or in silico work, clinical findings, or results from epidemiological studies carried out under other projects that will enable you to achieve your objectives. Consider including images (.jpg and .png files) of annotated flow charts and decision trees in your action plan to illustrate how objectives relate to each other.

We need a high- level overview of the scientific strategy to achieve the aim and each objective, including in vivo, ex vivo or non-animal studies that contribute to decision making of the in vivo work and/or realising the benefits. For example, in a drug discovery programme, initial identification of molecules that interact with the target will normally be done in vitro or from a literature search.

This section links the objectives to the protocols and explains how objectives will be achieved. There should be an outline of the stages of the programme of work and indication, using the protocol numbers, how each protocol will be used to achieve each objective.

Consider using an annotated flow chart, process map or decision tree with a short supporting narrative to summarise your strategic approach. This is often the clearest way of representing how the different objectives relate to each other and how the protocols will contribute to the objectives. Your process maps/decision trees can be uploaded and inserted as images (.jpeg or .png files). For each objective, indicate briefly what inputs (e.g., information, validated models & reagents etc.) are necessary and what outputs (for example data, models, or products) are expected. Where a programme of work has several sequential stages, explain the criteria for progressing to the next stage. Do not include detailed descriptions of the procedures or models at this stage.

An example of a process map is provided at the end of this section that illustrates the proposed work plan for a project investigating whether candidate genes have a role in energy and/or metabolic disorders. Note that the process map is based around the objectives the work is aiming to answer. It also shows the sequence of studies, work carried out prior to, and after this project, and the protocols used.

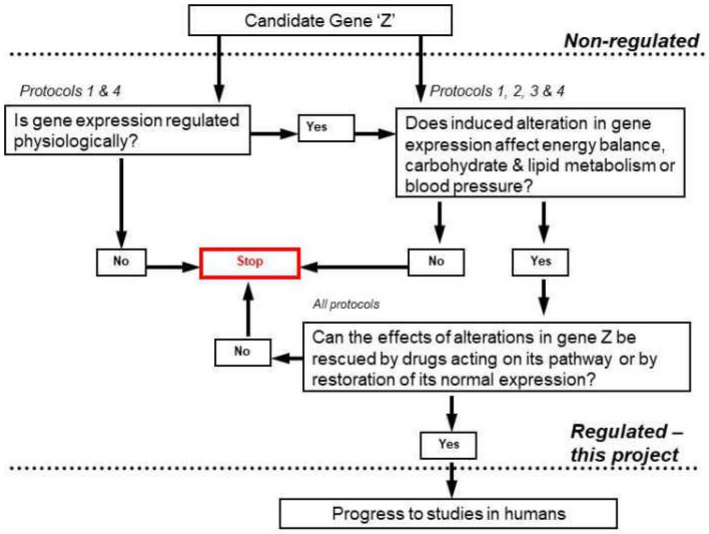
Whether or not you use a process map, add here a brief explanatory narrative to explain how decisions will be taken to determine how to navigate through the project. Show how and where the work of your project fits in with in silico, in vitro and ex vivo procedures and with work carried out under other projects or elsewhere.

Explain succinctly and in turn how each objective will be addressed and achieved. To do this, consider what output (i.e., data to be acquired, results or products to be generated) is needed to achieve the objective or the aim of the project as a whole.

Example of a simple GA mouse research project:

'To determine whether gene x plays a role in the development of diabetes, we will create mice that either don’t express the gene or overexpress the gene (which relates to clinical findings). We will use standard protocols 1-6 (superovulation, generation of founders, vasectomy, embryo recipient, breeding & maintenance mild and moderate). These mice will be used in a diabetes induction protocol (protocol 7) and the degree of development of diabetic signs will be measured.'

Decision tree example: Investigating whether candidate genes have a role in energy and/or metabolic disorders.



Where relevant, how will you seek to use or develop non-animal alternatives for all or part of your work?

Example: During the course of the project, we will continue to look for non-animal alternatives for any aspect of our work and we will use tools such as SyRF, the free online platform for researchers, to perform a systematic review and meta-analysis of animal studies.

Will you be producing data primarily for regulatory authorities that use standardised protocol frameworks?

Yes/No (Typically 'no' for purpose a, b, and non-regulatory purpose c)

Will you be undertaking non-regulatory testing or screening as a service to others?

Yes/No (Typically 'no' for purpose a, b, and non-regulatory purpose c)

Will you be producing genetically altered or surgically prepared animals/animal products using standardised protocol frameworks?

This includes projects to create, breed, maintain and supply genetically altered animals to researchers within the establishment, projects taking blood and other tissues for researchers and other clients within and/or external to the establishment.

Yes/No

Will you be manufacturing vaccines and medicines for medical or veterinary use?

Yes/No (Typically ‘no’ for purpose a, b, and non-regulatory purpose c)

General principles

Unnecessary duplication of work must be avoided. Under what circumstances would you knowingly duplicate work?

We need an explanation of steps taken to ensure testing you are doing will not duplicate tests already done or data already available. Replicating research findings of others might well be a legitimate part of a research programme.

Example: The genetically altered animals will be mice. Where suitable lines already exist, animals will be obtained from the relevant supplier. Otherwise, we will make the required lines ourselves (including conditional knockouts).

Example: Experimental reproducibility is an extremely important part of scientific investigation. Many experimental procedures involve technically demanding protocols, often using experimental reagents. It is essential that such experiments are repeated to provide confidence. Irrespective of power calculations, it is critical that experimental reproducibility is ensured.

Will all of your protocols or experiments use animals of both sexes?

Yes/No

Why will you use animals of a single sex in some protocols or experiments?

We require a robust explanation as to why animals of both sexes cannot be used. It is not enough to simply answer male mice fight so we will have to keep them singly housed or female mice result in high variability due to oestrus cycles. You need to explain why you cannot factor in sex differences (if any) into your experimental design. There are obvious exceptions e.g., studies on prostate cancer.

Protocols

The number of protocols required in a project licence depends on several factors including their purpose, procedures, animals, and harms. In general, multiple simple protocols provide greater clarity as to the harms that the animals will experience than a small number of complex protocols with lots of optional steps. Include multiple protocols if there are significantly different adverse effects, humane endpoints, species, or life stages with different capacities to suffer. Include separate protocols for model development and validation if the monitoring, controls, and humane endpoints are different. Endpoints identified during model development will inform the adverse effects for model use and should enable earlier or more refined humane endpoints when the disease model is used. Where different methods with similar adverse effects may be used to induce the same disease condition these can be included within the same protocol e.g., induction of diabetes using genetically altered mouse models (spontaneously diabetic) or streptozotocin. A protocol can be used to address more than one objective.

General constraints

Please note, constraints on procedures involving anaesthesia, surgery, substance administration and withdrawal of fluids apply to all protocols.

Anaesthesia

Induction and maintenance of general or local anaesthesia, sedation, or analgesia to mitigate the pain, suffering or distress associated with the performance of other regulated procedures is indicated using the following codes in protocols:

- AA no anaesthesia
- ABL local anaesthesia
- AB general anaesthesia with recovery
- AC non-recovery general anaesthesia
- AD under neuromuscular blockade

General anaesthesia

If authorised in this licence and unless otherwise specified, all animals are expected to make a rapid and unremarkable recovery from the anaesthetic within two hours. Uncommonly animals that fail to do so or exhibit signs of pain, distress or of significant ill health should be humanely killed unless a programme of enhanced monitoring and care is instituted until the animal fully recovers.

Surgery

If authorised in this licence and unless otherwise specified:

- Surgical procedures should be carried out aseptically;
- In the uncommon event of post-operative complications, animals will be humanely killed unless, in the opinion of a veterinary surgeon, such

complications can be remedied promptly and successfully using no more than minor interventions. Minimally inflamed wounds without obvious infection may be re-closed on one occasion within 48 hours of the initial surgery. In the event of recurrence, NVS advice will be followed;

- Peri and post-operative analgesia will be provided; agents will be administered as agreed in advance with the NVS;
- All animals are expected to make a rapid and unremarkable recovery from the anaesthetic within two hours. Uncommonly animals that fail to do so or exhibit signs of pain, distress or of significant ill health will be humanely killed by a Schedule 1 method unless a programme of enhanced monitoring and care is instituted until the animal fully recovers;
- Any animal not fully recovered from the surgical procedure within 24 hrs (eating, drinking and return to normal behaviour) should be humanely killed.

Administration of substances and withdrawal of fluids

If authorised in this licence and unless otherwise specified, administration of substances and withdrawal of body fluids will be undertaken using a combination of volumes, routes, and frequencies that of themselves will result in no more than transient discomfort and no lasting harm using published guidelines on minimal severity.

Protocol 1

Title

The title should reflect the purpose for which the protocol will be used and be reasonably short e.g., A murine model of inflammatory bowel disease (IBD)

Protocol 1: Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

By ‘regulatory guidelines’ we mean guidelines Regulators have published such as the OECD guidelines.

Provide a summary of the purpose of the protocol.

Example: Induction of colitis for the testing of novel IBD therapies

Example: To induce subcutaneous and metastatic tumours and study response to treatments

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Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

Select the appropriate prospective severity e.g., Moderate

What proportion of animals will experience this severity?

The severity category of the protocol is essentially a label that conveniently captures the maximum level of harm likely to be experienced (the worst case likely harms for each protocol – don't include unexpected events). The prospective severity must be determined using the principles at Guidance section 5.12 and Appendix G, and 'Severity classification of genetically altered animals under the Animals (Scientific Procedures) Act 1986'

Do not set the severity category until you have described the likely adverse effects of the individual procedures and their combined results, the control measures, and humane endpoints.

The final decision on the severity category for any protocol will be taken by ASRU. The Inspector will confirm that this is correct as part of their assessment. If this differs from the classification you have proposed, the application will be returned to draft on ASPeL for you to update and resubmit.

Licences with protocols classified as severe will be subject to Retrospective Assessment. See section 5.17 of the Home Office Guidance.

Example: 'Approximately 75% of animals are likely to experience moderate levels of severity. The remaining 25% of animals are likely to experience mild severity'.

Why are you proposing this severity category?

This section should include a description of the maximum level of harm likely to be experienced.

Example: We are proposing this severity category because 75% of animals will undergo surgery to occlude one ureter to induce inflammation in the associated kidney, repeated single housing in metabolic cages (once weekly for up to 12 weeks) and repeated blood sampling and dosing of substances. The remaining 25% of animals are likely to experience mild severity because they will not undergo the surgical preparation procedure and we expect the cumulative effect of the other procedures to be mild.

Locations where this protocol can be carried out

Select all that apply.

- Establishment 1

Which of your objectives will this protocol address?

Select all that apply.

- Translational research example: Determine the pathogenesis of the infectious organisms in pregnant and neonatal pigs

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Protocol 1: Animals used in this protocol

Mice

Which life stages will be used during this protocol?

Select all that apply

- Juvenile
- Adult

Will any animals coming on to this protocol be classed as 'continued use'?

'Continued use' describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

Yes/No. Further information regarding 'continued use' is available in the Home Office Advice Notes on Use, Keeping Alive and Reuse (Advice Note: Use, keeping alive and re-use).

How did these animals start their use?

Describe the procedures that have been applied to animals that will continue their use on to this protocol.

Continued use is an administrative way of specifying use over more than one project licence protocol within the same or different project licence(s). The regulated procedures authorised sequentially by the two (or, rarely, more) protocols must be essential to achieve the intended particular purpose. See Advice Note on Use, keeping alive and re-use.

For practical reasons, production of an animal model, e.g., breeding of genetically altered animals or surgical preparation may occur under a separate protocol from the subsequent experimental procedures applied to that model.

Transfer of animals between protocols for continued use in the same, or different, project licences must be authorised in the relevant parts of both protocols. However, the import (from outside the UK) of genetically altered schedule 2 species does not require specific authorisation as continued use as they have not been 'used' under the Act.

Example: Continued use of genetically altered mice: Mice for use in this protocol may be obtained from Protocol X of this project (Breeding and maintenance of genetically altered animals) or other projects with authority to breed and maintain genetically altered animals of that type and to provide them for use on other projects.

Example: Continued use of surgically prepared animals: Rats previously surgically prepared with one or more vascular cannulae at another licensed establishment under the authority of a Project Licence which permits transfer for continued use may be used in this protocol.

Will you be re-using animals on to this protocol?

'Re-use' describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

Yes/No

Describe any procedure that may have been applied to these animals, and why you are choosing to re-use them.

See the published Advice Note on Use, keeping alive and re-use.

Example: Wild-type genotyped animals from Protocol X (Breeding and maintenance of genetically altered animals) of this licence may be re-used.

Example: Dogs that have been kept alive and maintained under the supervision of the NVS at [place] may be re-used in this protocol, provided that all criteria in section 14 of the Animals (Scientific Procedures) Act and in this project, licence are fulfilled.

What is the maximum number of animals that will be used on this protocol?

Give a realistic estimate of the number of animals to be used in this protocol over the lifespan of the project.

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four. If no animals will go through this protocol more than once, enter '1'.

Where there is re-use on the same protocol the number will be greater than one.

Protocol 1: Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

Yes/No

Which general types or strains will you be using and why?

This series of questions is so that we can assess the justification for using GA animals, especially those that have an adverse phenotype.

- Where GA animals are expected to have a mild phenotype, the description can be general.
- For moderate or severe phenotypes, each genetically altered line or type of line must be specified.

Examples of mild phenotype:

- Immunodeficient mice [when held in suitable housing conditions] as hosts for implanted tumour tissue
- Zebrafish with genetic alterations relating to Y pathways to undertake work to achieve objective A
- Mice with tissue-specific fluorescent genes to allow localisation of [cell types]

Examples of moderate phenotype:

- Mice with alterations in x, y, z genes resulting in an increased risk of liver tumour formation
- Zucker rats as a model of non-insulin-dependent diabetes mellitus
- Mice with recombinant, mutant, knock-out or knock-down (constitutive or conditional) versions of x, y, z genes to study mechanisms of neurodegenerative disease.

Example of severe phenotype:

- Mice with a deletion or other alteration of gene x to identify the role of this gene in heart failure

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

Yes/No. Any harmful phenotype (spontaneous or induced) that is likely to be exhibited by GA animals on the protocol should be described.

Why are each of these harmful phenotypes necessary?

Ensure there is a robust scientific justification for any moderate or severe GAAs.

You should explain:

- Why the harmful phenotypes are necessary to achieve the objectives
- What other GA lines have been considered
- Why GAAs with a lower capacity to experience pain, suffering, distress, or lasting harm be used, such as fish, flies or worms are unsuitable.

How will you minimise the harms associated with these phenotypes?

Ensure that you include any humane endpoints that you will use.

This is for the Harm Benefit Analysis and to assess adequacy of refinement considerations.

Describe the harmful phenotypes and the refinement measures and other controls to minimise harms associated with these phenotypes.

Example: Animals will be killed before 12 weeks of age or at the onset of clinical signs if earlier unless required for experimental use when they will be transferred as continued use to Protocol X.

Protocol 1: Steps

Step 1 (mandatory)

A minimum of one step should be mandatory to aid in defining the purpose of the protocol. Any studies that do not use the mandatory step will need a separate protocol.

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g., dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g., use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

The rationale for each step must be clear, for example not 'administration of substances' by a number of routes but 'administration of potential therapeutic agents', 'administration of contrast agents', administration of antibiotics' or 'receptor agonists and antagonists', or 'administration of inducing agents'. Each route required should be listed. The exact substance to be used should be specified if it results in significant adverse effects. For example, DSS to induce colitis, CFA as an adjuvant.

Animal models with significantly different adverse effects should be authorised in different protocols, e.g., local benign tumours, malignant cancers, cancers of different organs, etc.

It is acceptable to write: 'unilateral nephrectomy (AB)'; 'Ovariectomy (AB)' etc. This allows for flexibility to use different more refined or more effective techniques without amending the licence. Related surgery, including surgical access and closure of the wounds, is encompassed by these general terms and does not need to be specified.

Be clear about control groups, including sham surgical controls - which steps will they go through? Specify if control substances will be administered.

Anaesthetic codes (AA, ABL, AB, or AC as appropriate to indicate when a procedure is being done under anaesthesia); or AD for procedures undertaken under neuromuscular blockade should be used for each step or sub-step. If administration of analgesia or anaesthesia (e.g., for restraint) is the only regulated procedure associated with an experimental step, this must be included as a separate step. It is helpful to provide details of the typical and maximal number, frequency, and duration of dosing.

For volumes, and for routinely used routes (like those listed in example below), it is acceptable to refer to published guidelines e.g., LASA, Diehl et al (2001) or Turner et

al (2011). However, it is still necessary to state frequency of dosing and the total duration of dosing to determine any cumulative effects that may raise the severity classification.

For less commonly used routes (e.g., intrathecal, intracerebral, intra-articular) or where limits vary from published guidelines, the maximum dose volumes, frequency and duration should be stated. The same applies to frequency and duration of repeated imaging, foot-shock etc. These details may be presented in a table in the Animal Experience section.

Sub-threshold procedures only need to be mentioned as a step if they might cumulatively result in above threshold levels of suffering. For example, repeated short periods of separation from cage-mates, repeated short periods of food restriction or some behavioural tests. These non-regulated procedures can be included as a step.

All protocols should include a final step that describes the fate of the animals (e.g., killed, kept alive) and method of killing to be used at the end of procedures or in the event an animal must be culled. Setting free to the wild during the course of procedures must be a step (see Advice Note: Working with Wild Animals).

Example: Removal of blood samples from a superficial blood vessel to assess haematological parameters (AA/AB/AC)

Example: Confinement/single housing in a metabolism cage (AA) usually up to 24 hours, but occasionally up to a maximum of 5 days.

Example: Immunotherapeutic substances or vehicle control will be administered alone or in combination by one or more of the following routes:

a) in the diet or drinking water continuously for up to two weeks (AA)

b) subcutaneous injection daily up to five times (AA/AB)

c) intraperitoneal injection daily up to three times (AA/AB)

d) implantation of a slow-release pellet subcutaneously on one occasion (AB)

e) topical application daily for up to one week (AA)

Is this step optional?

Yes/No (A minimum of one step should be mandatory)

Do you expect this step to have adverse effects for the animals that are more than mild and transient?

Do not list uncommon or unlikely adverse effects, or effects from procedures that will cause no more than transient discomfort and no lasting harm. For example, an intravenous injection of a small volume of an innocuous substance.

Yes/No

Where a step will cause adverse effects resulting in greater than momentary harm please select ‘yes’. Steps should typically include a description of adverse effects.

What are the likely adverse effects of this step?

State the expected adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

Common adverse effects, control measures and humane end points for surgery, anaesthesia, and substance administration are included as General Constraints in the licence and do not have to be repeated for these steps but it is helpful to reference the General Constraints in your response and provide any additional information.

Describe the expected adverse effects and their associated clinical signs including incidence. Do not describe unexpected adverse effects, which should be reported using the Standard Condition 18 form Project Licence Standard Condition 18 notification (publishing.service.gov.uk). General terminology can be used to describe the incidence of expected effects: rare (<1%), uncommon (1-5%), common (5-10%), usual, all.

Provide more detail for the procedures that cause the major impacts on animals.

Don’t forget to describe the expected adverse effects caused by the substances being administered. For example, chemotherapeutics or transgene inducing agents can result in adverse effects.

Regarding surgery, the standard general constraints text will cover the standard acute effects of surgery. Describe any longer-term consequences resulting from that surgery, e.g., neuropathic pain, stroke, liver failure.

Any adverse effects and humane endpoints relating to a GA phenotype will have been described in the GA animals section above and do not need to be repeated.

Examples:

Unilateral ureteral ligation will cause kidney inflammation in all animals which is not, in our experience, associated with signs of pain and although the affected kidney fails, the animal remains healthy because the other kidney functions normally. However, rarely animals may show signs of kidney failure (hunched posture, piloerection, abnormal drinking and eating).

Uncommonly, agents may cause skin inflammation, thickening or flaking, hair loss or altered pigmentation, benign cysts, skin erosions or tumours. When the reagent is applied to a pregnant female, these possible adverse effects might apply to the offspring.

Where tumours develop, the majority (~85%) are expected to be small epidermal tumours which will have no significant impact on the animal’s general well-being.

Repeated application of various agents in ethanol or acetone may occasionally cause excoriation of the skin.

How will you monitor for, control, and limit any of these adverse effects?

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

Monitoring must be specifically tailored for the procedure in question and take into account the stage or phase of the disease development and the rate of change of the animal's condition. Describe the frequency and timing of monitoring as well as the method of assessment (e.g., weighing, clinical scoring, calliper measurement). Clinical scoring sheets can be uploaded and included in the application in .jpeg or .png format but establishment guideline documents should not be referred to where they do not form part of the licence. External published guidelines should normally be considered when determining procedural steps and end points (e.g., LASA Guidelines).

Controls should include refinements such as specific husbandry measures (e.g., soft bedding, palatable and accessible diet, adapted housing or handling), medication (e.g., to limit seizures or control diabetes), or analgesia.

Limits are needed only where they impact directly on animal welfare. See general constraints for restrictions that will automatically form part of the licence. Examples of limitations include maximum dose or blood sample volumes (in ml/kg), maximum number of procedures, minimum intervals etc. You will need to detail how you will monitor animals post-surgery.

The limitations on severity and controls specified in this section need to be clear to personal licensees working under the project licence. They will use this information to judge whether they need to tell the PPL holder of a breach of severity under PIL SC 13 which may lead to a PPL SC18 notification. Animal care staff will use this information as a guide as to when to contact the personal licensee responsible for the animals, and as a guide to what action to take if no-one is available.

Example: Mice with arthritis will typically develop swollen joints that may limit mobility. Following the induction of arthritis, we will use refined care and housing of animals including soft bedding and nesting material and soft gel food. Mice will be examined each day and clinical symptoms of swelling will be scored for severity. Scoring will be performed on the ankle, hock and paws using a grading scheme (0 = normal; 1=swelling of one or more digits; 2=mild swelling of one or more joint; 3=severe swelling of entire paw or joint). Each limb will be graded and the total score for the animal determined (maximum score 12). If an animal reaches a score of eight or greater, it will be provided with analgesia following advice from the NVS.

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

End points should be specified in the licence. Endpoints should not be 'determined by the NACWO or NVS', although indicating when their advice will be taken is helpful (e.g., in the event of anaesthetic complications or post-surgical analgesia).

Humane endpoints should relate to the adverse effects. They should be relevant and justified i.e., if the protocol is classified as mild, the humane endpoints should not be set at moderate severity level.

If harms are seen, then endpoints should be set to minimise suffering but also enable scientific outputs to be achieved.

Example: Any animal displaying clinical signs of lethargy, piloerection, or hunched appearance for a period of 24 hours the animal will be humanely killed using a Schedule 1 method. In addition, any animal that loses 15% of its body weight compared to age matched controls will be killed.

Example: If the mean diameter of single tumours in rats exceeds 25mm the animal will be killed. Animals will be killed earlier if the tumour ulcerates or impedes any vital function (e.g., locomotion, vision, mastication, excretion). If a large number of small tumours or cysts accumulate in an area that impedes vital function, the animal will be killed.

Protocol 1: Fate of animals

What will happen to animals at the end of this protocol?

Select all that apply

- Killed

Will you be using non-schedule 1 killing methods on a conscious animal?

Yes/No

For each non-schedule 1 method, explain why this is necessary.

Answer YES to the question ONLY if the animal is conscious when it is killed e.g., decapitation of conscious neonates.

All methods of killing must be stated either in the protocol steps (e.g., a standalone step for decapitation) or as part of final killing step e.g., schedule 1 methods, exsanguination, completed by a schedule 1 method, perfusion fixation under terminal anaesthesia etc. The ‘Fate of animals’ section does not appear in the licence.

- Kept alive.

Animals are kept alive where you intend to re-use, set free or re-home the animal. A veterinary surgeon or another competent person must decide if an animal can be kept alive. Specific authority is required to subsequently re-use, set free or re-home the animal.

- Continued use on another protocol in this project

Please state the relevant protocol (for continued use).

Experimental protocols should typically not include continued use on to further experimental protocols.

Example: GA and wild type mice may continue to be used on protocols 2,3 and 5 of this project and on other projects with authority for continued use of animals of this type.

Example: Rat with a surgically implanted jugular catheter may continue to be used on other projects with authority to use animals of this type.

- Continued use on other projects

Protocol 1: Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

Describe the typical experience of an animal being used on this protocol. Where you have included optional steps, describe how these steps will be used and the maximal animal experience.

You can also explain here any general husbandry measures you will take to minimise contingent harms, such as housing NHPs in social groups.

Example: Mice are immunised with an immunogenic substance and/or a pathogen [descriptors]. In some cases, mice will be given test substances daily for up to a week, typically by one or two enteral or parenteral routes; on rare occasions by a maximum of three routes. Control animals may not receive any substance administration. Blood samples will be taken, typically weekly and all animals will be killed within 3 months of immunisation. The test substances will already have been tested to ensure that the dosing regimen does not cause toxicity.

Example: Animals will receive a stereotaxic injection of a viral vector expressing optogenetic constructs into the brain, followed by recovery time of 1 to 6 weeks. Animals should make an uneventful recovery. Then animals will be anaesthetised and decapitated for ex vivo brain slice preparation.

Example: Animals will typically undergo headpost implantation and intracranial injection (Step 2) before behavioural testing (step 4) and finally electrophysiology under terminal anaesthesia (step 5). In approximately 20% of experiments, animals will also experience transgene induction by tamoxifen (step 1) and surgical implantation of cannulae or electrophysiology probes (step 3).

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

General humane endpoints are an opportunity to summarise and describe the end points that are consistent across the steps of the protocol. They are typically in addition to those for each step and should limit cumulative harm. General humane endpoints may not be necessary if the humane endpoints are clear for each step and there is no cumulative or other harm. They should be relevant and justified (i.e., for mild protocol humane endpoints should not have suffering in moderate level) and should be consistent with the humane end points for each step.

Example of moderate severity general humane end points: Any animal that shows deviation from normal health (such as piloerection, hunched posture, abnormal gait,

inactivity or inappetence) with be monitored more frequently and supportive treatment provided such as warming and wet mash. Should the signs persist for a period of 24 hours the animal will be humanely killed using a Schedule 1 method. In addition, any animal that loses 15% of its body weight compared to age matched controls will be killed.

Protocol 1: Experimental design

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

Examples of outputs include tumour development and growth (rate of growth, volume, and number of metastatic sites); plasma cytokine levels; histological findings such as tumour vascularisation; genetically altered animals.

Example: The purpose of the protocol is to determine the potency of the test vaccine, which is calculated from the proportion of mice protected against toxin challenge in the test vaccine groups relative to the proportion of mice protected in the reference vaccine groups.

Will this protocol generate quantitative data?

Yes/No

Will your experimental design be determined by a regulatory guideline?

No

Where relevant, explain how and when pilot studies will be used.

Further advice available at NC3Rs Guidance on Conducting a Pilot Study. Any pilot studies that do not use the mandatory step will need either a separate protocol or be included as alternative (optional) step within the mandatory step.

How will you choose different experimental groups?

For example, controls, dose levels, satellites etc.

Example: The effect of anticancer drugs in animals with induced or implanted tumours will be tested typically at two, occasionally up to four, dose levels around the expected effective dose. Usually this involves no more than 3 animals per group. Doses will be adjusted when no effects, or rarely seen adverse effects, are observed. Unless there are good reasons otherwise, the experiments will be designed to compare dose levels.

How will you choose control groups?

Provide a robust scientific justification for controls with significant suffering such as sham surgery controls or untreated infected controls.

Clearly describe how control groups, including sham surgical controls, are used and the steps they will undergo. Provide a robust scientific justification for the use of sham surgical controls.

Example: Controls are needed in all experimental approaches to model confounding variables in common with the treatment group. We have considered confounding variables outside direct experimental manipulation include animal age, sex, microbiota, cage in which the animal is housed, room temperature and humidity. Control animals will be randomly allocated from the same pool of animals as treatment groups.

How will experiments and data analysis be randomised and blinded?

Example: We will make appropriate arrangements to randomly assign animals to experimental groups using block-randomisation tools (e.g., the NC3Rs EDA) and blind studies in accordance with the PREPARE guidelines and will plan and conduct studies to enable them to be published according to the ARRIVE guidelines.

How will you minimise variables to ensure reproducibility?

Example: Limit animal variation by using strains of the same background, age, and weight.

Example: Limit nuisance variables by standardising the time-of-day procedures are performed, or data are collected.

Example: Use standard protocols in experimental procedures and data analysis

How will you determine group sizes?

You should reference POWER calculations you have made, if relevant.

Power analysis is often useful in determining group size but not always applicable. Consider whether factorial designs are suitable. Specialist advice on experimental design and statistical analysis of results is usually widely available at establishments.

Example: Where relevant, factorial experimental designs will be used, rather than the one-thing-at-a-time approach, to maximise the information obtained from the minimum resource. For most of the quantitative experiments, sample sizes may be set using power analysis, generally using a significance level of 5%, a power of 80%, and a least practicable difference between groups of 25%. Otherwise, we will use our previous experience (ours, or from the literature) to select sample sizes. In terms of the numbers of animals required, we expect that 6 to 8 animals per treatment group should be sufficient to obtain the required results. However, because of the difficulty in obtaining satisfactory data from the very small dorsal root ganglion cells of C-fibre neurones, we expect to have to use rather greater numbers of animals per group to obtain satisfactory results: at this stage we are unable to provide a reliable estimate.

How will you maximise the data output from the animals you use on this protocol?

Example 1: Where possible up to three test vaccine batches are tested together in the same assay to maximise the use of the reference vaccine and control groups. Thus, minimising the use of animals overall.

Example 2: At post-mortem we will take and store as many tissues as possible and make them available to other researchers.

Protocol 1: Protocol justification

Why is each type of animal, experimental model, and/or method selected for this protocol:

a) the most appropriate scientific approach?

Scientifically justify the choice of animals (including species and life stage), the models, and methods in relation to the programme of work. Specific robust justification is required for severe procedures.

Example: We intend to use three models of peripheral neuropathic pain:

1) chronic constriction injury (CCI or Bennett model)

2) partial sciatic nerve ligation (PSL or Seltzer model)

3) L5/L6 (rat) or L4/L5 (mouse) spinal nerve ligation model (SNL or Kim & Chung model)

Each of these models has slightly different characteristic effects and we may need to use all of them to answer our particular scientific question. The SNL model has the advantages of a more consistent site and extent of ligation than the CCI or PSL models, and of having separate injured and intact spinal segments, but the disadvantage of requiring more extensive surgery.

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b) the most refined for the purpose?

Describe why each type of animal, experimental model, and/or method described in the protocol is the most refined approach to answering the scientific question. You may consult and refer to published guidelines to demonstrate evidence-based choices of models and ensure maximum model refinement e.g., IMPROVE guidelines for stroke models or other expert working group papers.

For each model and/or method, what is the scientific need for the expected clinical signs?

You need to explain the degree of pathophysiological changes that are scientifically necessary to achieve your scientific objectives. How do these correlate with the clinical signs in the animals? Why, scientifically, do the animals need to suffer to this degree? Why can you not achieve your scientific objectives with an earlier endpoint, or without the animals showing clinical signs at all?

Example: These are models of peripheral neuropathic pain and animals will show behavioural signs of spontaneous pain include guarding, excessive licking, and lameness in the ipsilateral hind paw. We require clinical signs of hyperalgesia and allodynia so that we can measure them and assess response to treatment.

Example: Animals will show clinical and behavioural signs. In our experience there is good correlation between hepatic immunophenotype and necroinflammation, and clinical signs such as temporary inactivity and affected gait. These clinical cues are more indicative of level of injury in the animals than serological parameters such as ALS/AST. We rely on these physical signs to demonstrate that individual animals are experiencing hepatic injury in response to their individualised treatment regimen.

Why scientifically do the animals need to suffer to this degree?

Example: The inflammatory nature of the model is such that to get clinically relevant results, some erythema and pruritus may be necessary. We aim for a model with the minimum of clinical signs while still allowing a positive response to treatment to be observed and quantified.

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

An example of a scientific endpoint would be blood glucose of > 300 mg/dl. Such animals would show some polyuria and polydipsia but no significant weight loss. A humane endpoint might be, for example, a hunched appearance with reduced locomotion or a particular score on a clinical/ welfare assessment sheet.

Will you be administering substances for experimental purposes?

Yes/No

How will you assess the suitability of these substances, and minimise the unnecessary harms arising from their administration given the particular strain or type of animal you will be using?

When assessing suitability, state how you will consider toxicity, efficacy, and sterility.

Examples include pilot studies, dose range finding studies, reliance on literature, using previous experience. Checks on potential toxicity and sterility are particularly important for novel test substances. How do you ensure suitability for administration into animals? e.g., in vitro tests, appropriate pH etc.

How will you determine an appropriate dosing regimen?

Include routes, dosage volumes, frequencies, and durations.

Describe how you will determine appropriate dosing regimens e.g., pilot studies, literature review, previous experience, or collaborators.

Example: If toxicity is unknown the substance will initially be tested in a pilot study. Dose setting, at a low dose in no more than two animals initially will be undertaken on a dose finding protocol. If no toxicity is seen, a further two animals may be tested at a higher dose and so on until an appropriate pharmacological dose level is reached. If the initial dose produces evident toxicity, doses will be reduced and retested.

Use of animals

Cats, dogs, and equidae

What are the scientific reasons for using cats, dogs, or equidae in your project?

A licence cannot be granted unless your scientific objectives or research questions can only be achieved or answered by the use of cats, dogs or equidae. This includes instances when it is not practicable to obtain other types of animals.

Explain why you need to use cats, dogs or equidae. A project licence cannot be granted unless the Secretary of State has verified that the purpose of the programme of work in the licence can be achieved:

- only by the use of cats, dogs or equidae; or
- only by the use of cats, dogs or equidae and other animals which it is not practicable to obtain.

The availability of background data or 'the usual species of choice' are not adequate justifications in themselves.

Note that applications proposing the use of cats, dogs, or equidae in procedures classified as severe or animals containing human material classed as Category 2 or 3 by the Academy of Medical Sciences will be referred to the Animals in Science Committee (ASC) for additional advice.

Non-human primates

Why do you need to use non-human primates, rather than any other type of animal, to achieve your objectives?

Explain why the purposes of the programme of work cannot be achieved by using species that are not primates.

Explain why the project is:

- translational or applied research for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man; or
- the development, manufacture or testing of the quality, effectiveness, and safety of drugs for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man; or
- basic research; or
- research aimed at preserving the species of animal subjected to regulated procedures.

Note that applications proposing the use of non-human primates in procedures classified as severe will be referred to the Animals in Science Committee (ASC) for additional advice.

Are any of these non-human primates endangered?

Endangered animals are any of the species listed on Annex A of Council Regulation 338/97 and are not bred in captivity.

Yes/No

Why can't you achieve your objectives by using non-human primates that are not endangered?

Also explain how you will comply with other regulations including CITES.

Provide relevant details.

Explain how the project is for one of the permitted purposes.

*The permitted purposes for the use of endangered non-human primates are: * translational or applied research for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man * the development, manufacture or testing of the quality, effectiveness and safety of drugs for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man * research aimed at preserving the species of animal subjected to regulated procedures.*

Applications that propose the use of wild-caught primates will be referred to the ASC for additional advice.

Might any of these non-human primates be wild-caught?

Yes/No

Why can't you achieve your objectives without using wild-caught non-human primates?

Applications that propose the use of wild-caught primates will be referred to the ASC for additional advice.

Purpose bred animals

Will all animals used in your project be purpose bred?

This means animals that have been bred primarily to be used in regulated procedures or for the use of their tissues or organs for scientific purposes.

Yes/No

Where will you obtain non-purpose bred animals from?

Consider the source of all animals you plan to use, as this information will help to assess the impact on the scientific output and the quality of the animal.

Provide scientific justification for using Schedule 2 species that are not purposed bred. Any non-Schedule 2 species should be from a source that can provide animals of a sufficient quality to produce satisfactory results.

Why can't you achieve your objectives by only using purpose bred animals?

A scientific reason is required for using non-purpose bred Schedule 2 species.

Endangered animals

Will you be using any endangered animals, apart from non-human primates?

Endangered animals are any of the species listed on Annex A of Council Regulation 338/97 and are not bred in captivity.

Yes/No

Why can't you achieve your objectives without using endangered animals?

Also explain how you will comply with other regulations including CITES.

Applications to use endangered animals will be referred to the Animals in Science Committee for additional advice.

Explain how the project is for one of the permitted purposes.

*The permitted purposes for the use of endangered animals are: * translational or applied research for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man * the development, manufacture or testing of the quality, effectiveness and safety of drugs for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in man * research aimed at preserving the species of animal subjected to regulated procedures.*

Provide relevant details.

Animals taken from the wild

Will you be using any animals taken from the wild?

Yes/No

Why can't you achieve your objectives without using animals taken from the wild?

In this context an animal ‘taken from the wild’ means a previously free-living animal that has been captured or otherwise brought under the control of man:

- whether or not it is to be kept in captivity for any appreciable length of time;
- whether or not it is physically taken away from the place of capture / ‘the wild’;
- whether a physical trap or device is used to take the animal, or any other means is used to bring it under the control of man (for example, picked up in the hand).

Special conditions apply to the use of animals taken from the wild and a variety of requirements (e.g., relating to capture, animals that are found to be injured or in poor health on capture) need to be covered in the answers below to ensure these are met. Stray animals cannot be used and there are restrictions on the use of other types of animals, such as feral animals.

The Advice Notes ‘Working with animals taken from the wild’, 'Re-homing and setting free of animals' and 'Use, keeping alive and re-use' also provide helpful information for animals taken from the wild.

Example: Wild rats are required as we are investigating the incidence of a rodenticide resistance gene in wild populations.

How will these animals be captured?

Explain how each method is the most refined for the animal type or purpose of the study. Also include any relevant considerations around trapping, including the frequency of checks and trap positioning.

Provide relevant details.

How will you minimise potential harms when catching these animals?

Provide relevant details.

Will your capture methods catch non-target animals?

Yes/No

How will you minimise the risk of capturing non-target animals, including strays and animals of a different sex?

Example: We capture birds only in nest boxes. The nest box entries are designed to only fit the species we want to catch. The nest boxes are checked on a schedule as to minimise disturbance for the bird. Only on a few occasions is another species present (e.g., nut hatch, bat), which we will not catch, but leave undisturbed until after the breeding season.

What will you do with any non-target animals that you capture?

Example: On the rare occasion other avian species are caught in the mist nets, they will be carefully checked and released immediately.

How will you ensure the competence of any person responsible for the capture of animals?

Example: Wild birds will be captured by people with a current BTO ringers' permit allowing unsupervised capture of the relevant species

How will you examine any animals that are found to be ill or injured at the time of capture?

Include details about what will be done with these animals after they have been examined.

Example: Assessment of injury and body condition will be carried out at the earliest possible opportunity after capture. This is done before the application of any regulated procedures. Birds will be weighed. Any bird with a weight that deviates negatively from the normal distribution will not be sampled (less than 20g for adult house sparrows)

Will a veterinary surgeon perform the examination?

Yes/No

How will you ensure the competence of the person responsible for making this assessment?

Describe the process for ensuring the person making the assessment has the necessary knowledge, skills, and competency to determine the appropriate action on capturing an ill or injured animal.

Is it necessary to use animals that are injured or in poor health during your project?

Yes

Explain why it is scientifically necessary to use animals that are injured or in poor health during your project.

Provide relevant details.

If sick or injured animals are to be treated, how will you transport them for treatment?

Include how you will ensure that any potential harms during their transport will be minimised.

Provide relevant details.

If sick or injured animals are to be humanely killed, which methods will you use?

Provide relevant details.

Will animals be marked, or otherwise identified, during the project?

Consider both regulated and non-regulated procedures in your answer.

Yes/No

How will animals be identified?

State which methods may cause more than momentary pain, distress, or lasting harm to an animal.

Provide relevant details.

Will any devices be attached to or implanted in animals during this project?

For example, any device used to identify, track, and monitor an animal's behaviour in its natural habitat.

Yes/No

How will any adverse effects from a device's attachment or implantation be minimised?

Examples include ensuring that any device is as small as possible or the use of break-away collars.

How will you locate and recapture the animals or otherwise ensure the devices are removed at the end of the regulated procedures?

If devices will not be removed, explain why it is not required.

Provide relevant details.

If animals will not have devices removed, what are the potential effects on them, other animals, the environment, and human health?

Provide relevant details.

I confirm that I have, or will have, all necessary permissions from other regulators in place before commencing any work involving animals taken from the wild.

Yes

Feral animals

Will you be using any feral animals in your project?

A feral animal is an animal living in the wild but descended from domesticated individuals.

No

Other considerations

Neuromuscular blocking agents (NMBAs)

Will this project involve the use of neuromuscular blocking agents (NMBAs)?

Yes/No

_____

Why do you need to use NMBAs in your protocols?

See Appendix H of the Guidance.

In addition, ensure that the use of neuromuscular blocking agents (NMBAs) is specified in the relevant protocol(s). You will need to show administration of neuromuscular blockers as a separate step and use the code 'AD' for all procedures conducted under neuromuscular blockade.

Ensure that the scientific need to use them is explained clearly in the action plan.

_____

What anaesthetic and analgesic regime will you use?

Provide relevant details.

_____

How will you ensure that animals have adequate ventilation?

Provide relevant details.

_____

How will you minimise pain, suffering, and distress for an animal under the influence of an NMBA?

Provide relevant details.

_____

How will you monitor the depth of anaesthesia?

Provide relevant details.

_____

How will you ensure there are sufficient staff present throughout the use of NMBAs (including during recovery periods) who are competent to use them in these types of animals?

You need to provide evidence of existing competence of staff or how such competence will be obtained.

Explain the agreed emergency routine at your establishment that covers potential hazardous events (such as a power failure).

Provide relevant details.

Re-using animals

Why do you intend to re-use animals?

Explain how you will balance the needs of refining and reducing animal use before making your decision.

Provide justification for re-use based on a positive balance of reduction and refinement.

What are the limitations on re-using animals for this project?

For example, there may be a maximum number of times that an animal can be re-used, or a set of performance standards that requires a limit on re-use.

Consider the welfare and scientific considerations that will be used to determine suitability for re-use and the criteria that will be used by the veterinary surgeon to determine that animals can be re-used, including any limitations on the period of time that the animal will be held under the supervision of the NVS/VS.

Describe controls on re-use, for example:

- maximum number of times; and/or
- performance standards e.g., patency of a cannula;
- humane end-points in the form of behavioural and/or physiological indicators that animals are suffering as a result of long-term laboratory housing or as a result of being re-used.

Commercial slaughter

Will you send any farm animals to a commercial slaughterhouse at the end of their use?

Yes/No

How will you ensure that these animals are healthy and meet commercial requirements for meat hygiene to enable them to enter the food chain?

Include any relevant information about drug withdrawal times.

Consider the requirements under ASPA section 17A. Complete the following:

<<<INSERT animal type(s) HERE>>> may be sent directly to slaughter at a registered slaughterhouse at the end of their use provided that:

- The animal is healthy and meets the commercial requirements for meat hygiene to enable them to enter the food chain. They must not be infected with any notifiable disease and comply with the relevant substance withdrawal times;
- While kept alive at <<<INSERT place HERE>>> pending transport to the slaughterhouse, the animal is kept in an appropriate social group under the supervision of a veterinary surgeon;
- The animal is appropriately identified and is transported in accordance with the relevant legalisation.

Animals containing human material

Do you intend to use animals containing human material in experiments classed as Category 2 or 3 by the Academy of Medical Sciences?

Yes/No

_____

Keeping animals alive

What types of animals will you keep alive?

See the Advice Note on Use, keeping alive and re-use.

Examples:

• Mice that have suffered actual severity that is no more than mild and are not suffering at the end of their use

• Dogs with implanted telemeters that are not expected to cause lasting harm

• Rats with implanted cannulae – for immediate transfer to the maintenance step in protocol x as re-use.

_____

What criteria will the veterinary surgeon, or competent person trained by a veterinary surgeon, use to determine whether animals can be kept alive?

Provide relevant details.

_____

Are there any limitations on the period of time that animals that have been kept alive can be held under the supervision of the veterinary surgeon?

Provide relevant details.

Setting animals free

How will an animal's health be assessed to determine whether it can be set free?

Complete the following:

<<<INSERT animal type(s) HERE>>> may be set free at the end of the series of regulated procedures conducted under the authority of protocol <<<INSERT protocol number(s) HERE>>> provided that the following actions have been taken:

- <<<INSERT actions to ensure the state of health allows the animal to be set free HERE>>>

Will a veterinary surgeon perform this assessment?

Yes/No

How will you ensure the competence of the person responsible for assessing whether animals can be set free?

Provide relevant details.

How will you ensure that setting animals free will not be harmful to other species, the environment, and human health?

- <<<INSERT actions to ensure that the setting free of the animal poses no danger to public health, animal health or the environment HERE>>>

Will you rehabilitate animals before setting them free? If so, how?

Provide relevant details.

Will you attempt to socialise any animals that you have set free? If so, how?

- <<<INSERT actions to ensure socialisation of the animal on being set free HERE>>>

How will you prevent inadvertent re-use of animals that have been released at the end of procedures?

Provide relevant details.

If animals are lost to the study or not re-captured, how will you determine whether your project is complete?

This information is important to ensure that the use of these animals is recorded in the return of procedures and is considered when determining the actual severity of your protocols.

Provide relevant details.

Rehoming animals

What types of animals do you intend to rehome?

Also state the protocols on which they would have been used.

<<<INSERT animal type(s) HERE>>> may be rehomed at the end of a series of regulated procedures provided that the following actions have been taken:

How will you make sure that an animal's health allows it to be rehomed?

<<<INSERT actions to ensure the state of health allows the animal to be re-homed HERE>>>;

How will you ensure that rehoming does not pose a danger to public health, animal health, or the environment?

<<<INSERT actions to ensure that the rehoming of the animal poses no danger to public health, animal health, or the environment HERE>>>;

What scheme is in place to ensure socialisation when an animal is rehomed?

<<<INSERT actions to ensure socialisation of the animal on being re-homed HERE>>>;

What other measures will you take to safeguard an animal's wellbeing when it is rehomed?

<<<INSERT any other measures to safeguard the animal's welfare on being re-homed HERE>>>.
