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NON-TECHNICAL SUMMARY

# Clinical veterinary studies of naturally occurring disease in animals (III)

**Project duration**

5 years 0 months

**Project purpose**

- (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

**Key words**

clinical trial, veterinary, spontaneous disease

| Animal types | Life stages |
|---|---|
| Other dogs -Doberman | adult |

## Retrospective assessment

> The Secretary of State has determined that a retrospective assessment of this licence is required, and should be submitted within 6 months of the licence's revocation date.

**Reason for retrospective assessment**

This may include reasons from previous versions of this licence.

- Uses cats, dogs or equidae

# Objectives and benefits

**Description of the projects objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.**

**What's the aim of this project?**

To permit the ethical conduct of phase II to IV clinical trials of new drugs, devices and techniques in client owned animals attending a veterinary setting.

**A retrospective assessment of these aims will be due by 06 November 2027**

The PPL holder will be required to disclose:

- Is there a plan for this work to continue under another licence?
- Did the project achieve it's aims and if not, why not?

**Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.**

**Why is it important to undertake this work?**

The benefit of this  project licence is rapid progress of the development of novel therapies/techniques in the management of disease in client owned animals. There are a wide range of unmet veterinary needs, requiring new drugs/devices to be developed as approved veterinary medicinal products and new diagnostic techniques.  This licence seeks to improve the treatment of spontaneous disease in client owned animals.

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

The primary data outputs will be clinical, clinicopathological, histopathological, diagnostic imaging data to support or refute development and use of new drugs, devices or diagnostic techniques for the management of spontaneously occurring disease in client owned animals.  Data will relate primarily to clinical efficacy, safety and underlying biological mechanisms and will:

● enable an objective decision to be made regarding whether or not to progress a novel therapy or technique through further stages of product development

● provide an understanding of any potential adverse effects and allow for appropriate contraindications and precautions in any subsequent clinical trials

● increase the number of novel safe and effective treatments and diagnostic tests available for a range of conditions affecting companion animals.

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

The benefit of this Project Licence is rapid progress of the development of novel therapies/techniques in the management of disease in client owned animals attending a veterinary setting. There are a wide range of unmet veterinary needs, requiring new drugs/devices to be developed as approved veterinary medicinal products and new diagnostic techniques. This Licence seeks to improve the treatment of spontaneous disease in animals.

Individual animals recruited to the studies will have their disease well defined and throughout the studies their progress will be closely monitored, resulting in a direct benefit to every animal recruited.

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

Data will be reported and published for use by:

- Pharmaceutical companies/Sponsors to progress development of novel therapies/techniques including licencing for new indications,

- Veterinary surgeons to promote evidence-based medicine in clinical practice

Additional benefits include the collection and storage of blood, urine and tissue samples for animals with specific diseases. Analysis of the samples could lead to the identification of potential new biomarkers of disease and facilitate genomic and metabolomic profiling for mechanisms of disease and identification of new therapeutic targets. These secondary benefits will be used by veterinary researchers to further our understanding and treatment of veterinary diseases.

**Species and numbers of animals expected to be used**

- Other dogs: No answer provided

# Predicted harms

**Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.**

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

Client-owned animals used in these studies will be selected based on the spontaneous disease being targeted for treatment. Age, sex / breed will be set to reduce variability between animals and ensure the level of disease is standardized where possible across the study.

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

Client-owned animals that have been referred to the veterinary clinic with appropriate spontaneous naturally occurring disease will be enrolled on to studies. The owner will sign an animal consent form

to allow their pet to be assessed for enrolment on the study.

The animal will generally experience normal veterinary work-up and interventions for the treatment of their disease. Then a new therapy, supplement or device may be administered in conjunction with the gold standard treatment, with the aim of improving animal recovery/ outcomes. Only those studies approved by the Veterinary Medicines Directorate will allow a new therapeutic treatment to replace current licensed therapies.

Typically, the regulated procedures performed under this PPL will be the extra sampling required to show efficacy of the product or device being tested eg a series of blood samples collected for monitoring drug levels or a follow-up imaging session performed under general anaesthesia to assess the effectiveness of a new product.

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

The impacts of the regulated procedures on these client-owned animals are typically expected to be mild and transient when performing blood sampling or fluid sampling procedures only.

Those protocols involving injection of novel substances (with or without general anaesthesia), biopsy procedures or imaging are classed as moderate. Animals will be monitored closely by veterinary professionals during recovery and are only discharged from veterinary care when they are fully recovered from the procedure and any anaesthesia. Possible, but unexpected, adverse effects include; anaesthesia recovery complications, allergic response to injection, pain or infection which will most likely be observed and treated before the animal is discharged from the veterinary clinic.

**Expected severity categories and the proportion of animals in each category, per species.**

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

All animals completing a study should experience the same severity based on the sampling protocols and expected adverse events under this PPL we would expect the following:

Dogs >90% Mild <10% Moderate

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

- Rehomed

**A retrospective assessment of these predicted harms will be due by 06 November 2027**

The PPL holder will be required to disclose:

- What harms were caused to the animals, how severe were those harms and how many animals were affected?

# Replacement

**State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.**

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

The primary purpose of this Licence is to improve the health of client-owned animals with spontaneously occurring diseases. Effectiveness of a new treatments require robust testing under controlled conditions in the target animal showing symptoms of the relevant disease prior to acceptance/ approval as a new veterinary treatment.

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

Effectiveness of a new treatments require robust testing under controlled conditions in the target animal showing symptoms of the relevant disease prior to acceptance/ approval as a new veterinary treatment. Whilst non-animal alternatives may be used during product development this cannot replace the use of animals for efficacy testing in the target animal.

**Why were they not suitable?**

There is a need to perform controlled veterinary clinical trials for novel therapies / techniques for treatment of animals in the target animal.

**A retrospective assessment of replacement will be due by 06 November 2027**

The PPL holder will be required to disclose:

- What, if any, non-animal alternatives were used or explored after the project started, and is there anything others can learn from your experience?

# Reduction

**Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.**

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

Each study is individually assessed and predicted animal numbers indicated on the relevant project protocol.

Review of historic veterinary clinical data can predict outcomes of spontaneous disease standard therapies when planning new studies.

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

All clinical efficacy studies will be assessed by a statistician to ensure the minimum number of animals based on standard power analysis with Bayesian considerations and will make use of bias avoidance methods, adaptive study design and interim analyses to facilitate sound decisions on whether to stop or continue treatments or terminate the study. Cross-over designs will be considered to reduce total number of animals required with a suitable wash-out period.

These studies are uniformly looking for marked or “clinically significant” effects: the number of animals required to show a large effect are smaller than if the study end-points were more subtle.

Variability will be reduced by studying animals with specific disease and excluding animals with co-morbidities where possible.

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

Review of historic veterinary clinical cases will be used to predict outcomes of spontaneous disease with standard therapies when planning each study.

Ensuring a good study plan and data capture forms are prepared will ensure optimal data is gathered for each animal to contribute to the study.

Some blood and tissue archives are available as a resource for researchers.

**A retrospective assessment of reduction will be due by 06 November 2027**

The PPL holder will be required to disclose:

- How did you minimise the numbers of animals used on your project and is there anything others can learn from your experience?

# Refinement

**Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.**

**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.**

Client owned animals with defined specific spontaneous diseases will be used in these studies with the primary aim of conducting clinical trials of drugs/devices/techniques of these disease in these species. An alternative is therefore not an option.

A thorough review of all known adverse events of all drugs/devices/techniques to be tested will be conducted prior to commencement of studies to facilitate specific close monitoring for any expected adverse events.

If the specific target disease progresses despite study procedures, or other co-morbidities occur that are likely to compromise the study, then animals may be withdrawn from ASPA and returned to the care of the Owner and Veterinary Surgeon so that an appropriate treatment plan can be agreed under the Veterinary Surgeons Act.

All animals will remain under the care of their owners while enrolled on the study: their emotional and welfare needs will be taken care of in their own home. Regulated procedures will take place at the Veterinary Clinic to the highest standards of welfare and patient care and supported by 24/7 dedicated veterinary professional support.

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

There is a need to perform clinical trials of novel treatments / techniques in animals of the same status for which the product/ techniques is intended.

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

This PPL is performed within a world class veterinary teaching hospital where veterinary and veterinary technical support staff are required to keep up to date with CPD to advance their knowledge. Advice will be sought from these people when designing the study plan.

Any relevant post procedure care and monitoring will be performed by veterinary professionals until the animal is deemed fit to be released from the Act by the attending veterinary surgeon.

Where appropriate sedation, and/or local or general anaesthesia will be used to minimise stress or pain during procedures.

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

Veterinary surgeons and veterinary nurses involved in these studies are all required to perform regular CPD to maintain the highest standards to maintain their professional registration.

Best veterinary practice will be employed at all times.

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

NC3R website will be used as a source of information of advances in 3Rs, as well as review of the regular updates received from the designated establishment. Any advance considered appropriate in this PPL will be incorporated into the in-vivo experiments where possible.

Regular updates from the NC3R website are circulated by the establishment's AWERB.

**A retrospective assessment of refinement will be due by 06 November 2027**

The PPL holder will be required to disclose:

- With the knowledge you have now, could the choice of animals or model(s) used be improved for future work of this kind? During the project, how did you minimise harm to the animals?