

## G: NON-TECHNICAL SUMMARY (NTS)

Please attach the Non-technical Summary as generated by your application in ASPeL.

NOTE: The Secretary of State considers the provision of a non-technical summary (NTS) is an essential step towards greater openness and requires one to be provided as part of the licence application in every case. You should explain your proposed programme of work clearly using non-technical terms which can be understood by a lay reader. You should avoid confidential material or anything that would identify you, or others, or your place of work. Failure to address all aspects of the non-technical summary will render your application incomplete and lead to it being returned.

This summary will be published (examples of other summaries can be viewed on the Home Office website at [www.gov.uk/research-and-testing-using-animals](http://www.gov.uk/research-and-testing-using-animals)).

Word limit; 1000 words

<b>Project Title</b>	How does sinus node disease maintain atrial fibrillation? A mechanistic study of electrical and structural remodelling
<b>Key Words</b>	atrial fibrillation, arrhythmia, heart
<b>Expected duration of the project</b>	5 year(s) 0 months

### Purpose of the project (as in ASPA section 5C(3))

#### Purpose

**Yes** (a) basic research;

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

**Yes** (i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants;

**No** (ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants;

**No** (iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.

**No** (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 aims mentioned in paragraph (b);

**No** (d) protection of the natural environment in the interests of the health or welfare of man or animals;

**No** (e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work;

**No** (f) higher education or training for the acquisition, maintenance or improvement of vocational skills;

**No** (g) forensic inquiries.

**Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):**

Atrial fibrillation is the commonest sustained heart rhythm problem and leads to reduced quality of life and risk of stroke. It is harder to treat when the normal pacemaker of the heart (the sinus node) is also diseased.

This project aims to investigate why sinus node disease makes atrial fibrillation harder to treat and to take steps towards developing personalised treatments for these patients.

**What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?**

Improved understanding of the interaction between sinus node disease and atrial fibrillation will allow us to be able to design different treatment techniques to improve the outcomes in these patients. It will also provide additional knowledge that will allow us to take steps towards testing gene therapy for the treatment of these diseases.

**What types and approximate numbers of animals do you expect to use and over what period of time?**

We will use up to 20 goats over 4 years

**In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected levels of severity? What will happen to the animals at the end?**

The animals will have pacemakers implanted under general anaesthetic. During recovery from this operation they will suffer moderate levels of pain and discomfort which will be controlled using painkillers. The pacemakers will be used to cause atrial fibrillation in 8 of the animals and, depending how they respond some of these animals may feel out of breath. If this happens they will receive treatment from a Vet. After 12 weeks, the animals will have a general anaesthetic and the electrics of the heart will be measured in detail. While still asleep they will be humanely killed and the heart will be removed for further microscopic analysis. During the course of the study, if any of the animals are seen to be in pain, or distress that can not be treated they will be humanely killed.

## **Application of the 3Rs**

### **Replacement**

State why you need to use animals and why you cannot use non-protected animal alternatives

### **Replacement**

Computer models of atrial fibrillation are under development, but the heart rhythm disorder is not completely understood and one of the aims of this project is to advance this knowledge. We already work with a computer modelling group to develop computer models of heart rhythm disorders and the data from this research will be shared with the computer modelling group to help further advance these

models. Some research will be done on humans during surgery or cardiac procedures, but to understand the causes of the electrical abnormalities tissue samples need to be analysed for scarring or disarray and it is not possible to take these samples from humans.

### **Reduction**

Explain how you will ensure the use of minimum numbers of animals

### **Reduction**

The experimental design has been discussed with a statistician to ensure that the minimum number of animals will be used while ensuring sufficient statistical power for meaningful results.

### **Refinement**

Explain the choice of animals and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.

### **Refinement**

The study of complex heart rhythms like atrial fibrillation require study of a heart that is of a similar size to humans so results are translatable. This is because the nature of heart rhythm patterns are affected by the size of the heart, so results from small animals are not as relevant. Prior studies of atrial fibrillation in goats and sheep have detected electrical signals that are very similar to those seen in humans and have advanced the understanding of human atrial fibrillation.

The number of procedures performed on each animal is being kept to an absolute minimum and any painful procedures performed during this study will be performed under anaesthetic and with rigorous pain relief as advised by a veterinary surgeon. The goats will be kept in an environment where they will be able to express their normal behaviour so they will have the facility to climb and to live in groups. The animals may occasionally need to be on their own for short periods, but this will be kept to an absolute minimum. They will be frequently monitored for signs of distress or illness and will be treated promptly should these be observed.