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G. NON-TECHNICAL SUMMARY (NTS)

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.

Word limit; 1000 words

Project Title	Understanding inflammasome dependent inflammation
Key Words	Inflammation, Disease, Injury, Infection
Expected duration of the project	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):

Here we aim to understand the regulation of an organisms inflammatory response to infection or injury. The inflammatory response is how our immune system reacts to a stress or danger. There are particular components of this response that are now known to contribute to disease (called the NLRP3 inflammasome) but we do not know fully how this is works. The objectives of this work are to understand how the inflammasome (in particular NLRP3) works, to identify molecules that can stop it working.

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)?

This project will advance our basic understanding of life processes and will aid the identification of potential new therapies for the treatment of inflammatory disease.

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

Mice (1800) and rats (350) will be used over a 5 year period.

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 severity is moderate and the animals will only experience temporary discomfort. The impact will be similar to what humans experience when sick with an infection, but will usually only last for a few hours before the animals are sacrificed to take tissues for ex vivo analysis.

Application of the 3Rs

Replacement

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

Replacement

Inflammation is a complex vascular and cellular response that cannot be modelled accurately in *in vitro* systems. The proposed studies could also not be undertaken in lower species because they do not show such similarities to humans (e.g. do not have NLRP3).

Reduction

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

Reduction

Several factors lead to a reduction of animal numbers, including reducing variation and good experimental design involving the use of appropriate statistics. In particular statistical tests will be used to ensure that we use the minimum number of animals possible to reliably interpret our data.

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

Mice and rats are the lowest vertebrate species that share common pathways to humans with respect to this pathway. We will use well-established methods to cause inflammation without causing severe or long lasting harm to the animals. Sometimes we will test the behaviour of the animals but the tests we will use do not cause any distress or lasting harm and usually rely on natural behaviour of the animals (exploration, social interaction) However, all animals will be constantly monitored to ensure that they suffer minimum distress.