Private & confidential: *Please be aware that the contents of this form may be made public resulting from the "Freedom of information Act". Personal details will not be released.*

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	Drug discovery for parasitic helminths
Key Words	Drugs, Parasites
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):

Gut dwelling parasitic worms are extraordinarily common impacting on the health and wellbeing of around one quarter of the world's population. Drugs currently used to treat these types of parasite are losing their effectiveness therefore new drugs are urgently needed.
Aims: The project aims to discover new drugs and assess the possibility of using existing drugs, currently used for the treatment of other diseases, as anti-parasite therapies.

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)?

In the short terms we will publish our work and discuss our data at scientific conferences. This will facilitate sharing of our compounds with other researchers who will be able to test them against other types of infection. In the long term, the discovery of new drugs to kill parasites will significantly help in controlling parasitic worm infections in developing countries. Within 5-10 years it is highly likely that we will have discovered and optimised, through chemical modification, new anti-parasitic drugs suitable for clinical trials in man and/or use in veterinary applications.

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

We will work with adult mice and expect to use 2740 over 5 years. A total of 2740 mice gives us the potential to identify up to 17 new chemicals for use as new anti-parasitic drugs.

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 procedures employed under this licence are classified as moderate. There are two main possible harmful effects, the first relating to administration of the new chemicals and the second to removing of blood samples. Both are expected to be rare events (<0.1%). Protocol 1. Mice will be treated with new chemicals orally, or by an injection in to the abdominal cavity or into the blood stream, or under the skin. As these are new chemicals it is possible that, occasionally, the mice will react badly to these chemicals. We expect these to be very rare events (<0.1%) as any chemical administered to mice will have gone through rigorous testing in vitro to show that they do not kill cells. Mice will be checked daily after treatment with the new chemical. We will look for signs that the animal is beginning to suffer and any mouse affected will be humanely killed. Protocol 2. Chemicals which are well tolerated by mice in protocol 1 will then be used in protocol 2 which will enable us to establish how long the chemicals last in the bloodstream and the ability of the chemicals to eliminate the parasite from the mouse. In order to do this, mice will be infected with parasites using standard procedures, chemicals administered and blood repeatedly withdrawn from a tail vein. The main risk of harm to the mouse in protocol 2 is excessive blood loss. We expect loss of too much blood to be very rare (<0.1%) as we will carefully control the frequency and size of the blood sample taken. We will ensure bleeding has stopped after each sampling. If the bleeding cannot be controlled, resulting in a blood loss greater than defined limits, the mouse 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

Chemicals will be tested in vitro first, and only those chemicals which kill the parasite in vitro will be tested in vivo. Thus the work involving animals will be considerably reduced. However it is necessary to determine whether the chemicals show anti-parasitic activity in vivo

Reduction

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

Reduction

We will not only test new chemicals but also test to see if we can use existing drugs, developed for different purposes, to kill parasites. In these situations where possible we will use existing data which will tell us (a) if the chemical has caused harmful effects in mice before and at what dose, and (b) how the drug behaves in the body. This will reduce animal usage.
One of our key goals is minimisation of variation; this is pivotal in determining the number of animals required to demonstrate a real reduction in the number of parasites after chemical treatment. For example we will:

- Use the same strain of mice, purchased from a single supplier with minimum variance in weight
- Use the same personnel, familiar with each step of the model
- Study multiple compounds within one experiment, minimising the number of untreated control groups.
- Calculate sample size based on available data before the experiment.

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

Our studies focus on the infection of laboratory mice with the parasite Trichuris muris. Trichuris trichiura is the equivalent parasite that infects man and it is virtually identical to Trichuris muris. Thus the mouse model enables us to develop new therapies to treat Trichuris trichiura in humans.
The protocols employed are well established in our lab and designed not to induce suffering in animals.