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	Brainstem circuits controlling gut-brain communication
Key Words	eating habits, gut, brain network, obesity, intestinal health
Expected duration of the project	2 year(s) 10 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;
Yes	(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):

The objectives of this Project Licence are centred on the regulation of the gut-brain interaction, and how visceral information are received and computed by discrete groups of nerve cells to maintain health. To achieve this, we take advantage of genetic engineering techniques to precisely interrogate the function and the chemical content of discrete brain cells and to correlate these specific cell manipulations to changes in brain or gut health.

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)?

The primary benefit of the work will be the advancement of scientific knowledge on the logic by which the brain compute and store messages sent by the gut. These knowledge will be directly relevant for human and animal health and welfare. For example, in humans there is high co-morbidity of obesity, gastrointestinal and psychiatric diseases (i.e. anxiety, obsessive compulsive disorders, and depressive states). Understanding how the communication between the gut and the brain is regulated may have implications for the health and wellness of animals (including humans), in that it will provide an evidence base for the development of novel pharmaceutical, behavioral or nutritional intervention to treat or diagnose brain and gut diseases.

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

This program of work may use 4000 mice over 5 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?

Mice may be injected with physiological doses of hormone or pharmaceutical agents. This is a mild procedure that very rarely promotes adverse effects. In some cases, treatments may lead to reduced body weight. Some mice may experience surgery. Possible pain is minimised by good surgical and aseptic techniques, suitable anaesthesia, good perioperative care and adequate provision of pain relief. This is a moderate procedure. Likewise, some mice may experience gastrointestinal discomfort when subjected to experiments mimicking the human intestinal bowel disease. All other procedures involve the monitoring of natural behaviour, including eating habits; procedures that never promote adverse effects. Any animal showing any signs of ill health will be closely monitored, receive veterinary treatment or will be humanely euthanized. At the end of testing, mice will be humanely euthanized for tissue and data collection.

Application of the 3Rs

Replacement

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

Replacement

Animals are the only model for the proposed licence because it is not possible to study gut-brain communication using cultured cells or computer modelling. At present, to understand how these two distinct, yet tightly connected, body districts interact requires the use of live animals. However, the research programme seeks to identify means for replacement by incorporating mathematical modelling when available, and basic knowledge that will be acquired with this program of work also have the potential to facilitate replacement.

Reduction

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

Reduction

Sample sizes will be based on statistical power analysis from several prior experiments and power calculations conducted with a statistician. Sample sizes will be reduced to include the minimum number of mice necessary. Built into the experimental design and dissemination of the results are the ARRIVE guidelines established by the NC3Rs. Measures taken to avoid unjustified duplication of procedures will include close monitoring of literature; conference attendance and discussing current procedures with colleagues and veterinary staff.

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 mouse is the species of choice. There is a large scientific literature on this species and other alternative models do not allow for precise genetic manipulations of brain cells during enacted behaviour. Refinements for injections include the implementation of scoring sheets and humane endpoints. Pain and suffering is minimised by good surgical and aseptic techniques, suitable anaesthesia, good peri-operative care and adequate provision of pain relief. To prevent duplication of experimentation, scientific conferences are attended and discussion held with colleagues. The scientific literature is continually reviewed and veterinarians consulted for alternative surgical treatments and novel means to alleviate adverse effects.