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 project clearly using non-technical terms which will be understandable to 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 may 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 http://scienceandresearch.homeoffice.gov.uk/animal-research/).

(WORD LIMIT: 1000 WORDS)

Please complete the following:

<table>
<tr><td>Project Title (max. 50 characters)</td><td colspan="3">Regulation of pituitary physiology</td></tr>
<tr><td>Key Words (max. 5 words)</td><td colspan="3">Pituitary, gene regulation, prolactin</td></tr>
<tr><td>Expected duration of the project (yrs)</td><td colspan="3">5</td></tr>
<tr><td>Purpose of the project (as in section 5C(3)[1]</td><td colspan="3"><table>
<tr><td>Basic research</td><td>Yes</td><td></td></tr>
<tr><td>Translational and applied research</td><td>Yes</td><td></td></tr>
<tr><td>Regulatory use and routine production</td><td></td><td>No</td></tr>
<tr><td>Protection of the natural environment in the interests of the health or welfare of humans or animals</td><td></td><td>No</td></tr>
<tr><td>Preservation of species</td><td></td><td>No</td></tr>
<tr><td>Higher education or training</td><td></td><td>No</td></tr>
<tr><td>Forensic enquiries</td><td></td><td>No</td></tr>
<tr><td>Maintenance of colonies of genetically altered animals[2]</td><td>Yes</td><td></td></tr>
</table></td></tr>
<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td colspan="3">The pituitary gland produces hormones that control a wide range of body functions. Hormone production is regulated both acutely in response to immediate stimuli such as stress and trauma, and also chronically in response to physiological changes like puberty and pregnancy. It has been found that gene expression in the pituitary is dynamically variable, both in tumour cell lines in vitro, and in normal animal tissue. We are exploring the mechanisms and significance of the dynamic responses of gene transcription in living cells, and how this relates to pituitary growth and development. An important aspect of this work is the ability to study normal pituitary tissue, as opposed to cancer cell lines.
Transgenic rats are available in which marker genes are expressed in the pituitary gland. These marker genes have no detrimental effect on the pituitary gland itself or on the animal's well being, but allow us to study the behaviour of pituitary tissue that has been removed from the animal after</td></tr>
</table>

[1] Delete Yes or No as appropriate.
[2] At least one additional purpose must be selected with this option.

	death.
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 work will lead to new understanding of the role of tissue structure in coordinating the production of hormones in normal physiology. This in turn will help us understand how tumours arising in the pituitary gland over-produce these hormones, and we hope it will contribute to the development and understanding of new therapies for these tumours in man.
What species and approximate numbers of animals do you expect to use over what period of time?	Rats and mice, up to 4000 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 level of severity? What will happen to the animals at the end?	Very few if any adverse effects are expected. Most of our studies will be aimed at normal physiology in healthy animals, for example during early development, pregnancy and across the oestrous cycle. In some experiments we will study the effect of oestrogen, using hormone implants similar to those used by women in routine healthcare. Discomfort from oestrogen implant administration will be minimised with analgesia. In rats, oestrogen administration can cause weight loss, and weight will be carefully monitored, and experiments terminated if weight loss exceeds 15% - in most cases the severity limit is likely to be mild, with a maximum severity limit of moderate. Animals will be humanely killed at the end of experiments.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The aim of the work is to study effects of tissue structure on hormone production. Cancer cell lines have been studied until now, and limited work can be performed in this way on individual cells, but for analysis of tissue structure animal work is essential.
2. Reduction Explain how you will assure the use of minimum numbers of animals	We are using microscopic approaches studying the behaviour of individual cells, and this allows us to minimise the numbers of animals to ensure reproducibility of results consistent with achievements of scientific goals.
3. Refinement Explain the choice of species 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.	We are using laboratory rodents as these are amenable to genetic manipulation, and the physiology of the pituitary gland is well understood. Animals are observed at least once a day. No adverse effects are expected from the endocrine manipulations. Analgesics will be administered after surgical procedures to minimise discomfort or pain, and we will seek veterinary advice if we encounter any unexpected occurrences.
For Office Use Only	
Will the project be subject to Retrospective Assessment?[1]	Yes | No | Date due[3]:

[3] The retrospective assessment should be completed, agreed with the establishment AWERB, and submitted to the Home Office within 3 months of this date (or when the project terminates if earlier).