

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	Designing therapeutic and diagnostic nanotechnologies for medicine
Key Words	Nanomaterials, Preclinical, Therapeutics, Diagnostics, Recording
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.

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.

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

In the clinic, there are many drugs available to treat diseases, but often delivering the treatment to the right place is difficult. There are also some diseases, such as Parkinson's disease or epilepsy, where either the current treatments or the best strategies to diagnose a disease are not good enough for all patients. Using expertise in the fields of chemistry, engineering, pharmacy and biology, the Nanomedicine Lab will design and test new materials or devices, and compare them with what are used treating patients currently. The use of nanomaterials, seeks to design smarter solutions, as the nanomaterials themselves can be engineered with different properties such as size, electrical charge and shape. Nanomaterials are any materials which have a size in the range of nanometres, the same scale as the DNA within cells. We aim to test the safety of the materials or devices, first in cells grown outside the animal, and then in healthy animals, before moving on the use in disease models to test their effectiveness.

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 benefits of this programme of work are mainly centred on improving the tools available to treat a wide range of diseases. While the license focuses on a few specific diseases, the tools and techniques being designed are applicable in many scenarios. This means that once a design is shown to be safe and work for its intended function, it could be tested in many other diseases. As well as the clinical implications, there is also a great deal we can learn about the materials themselves. By studying where the materials go in the body and how the body reacts, we can learn about their safety, which will inform other researchers interested in using the same tools. It will also inform health and safety protocols for those who may be exposed to nanomaterials such as during their jobs.

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

The work in this license will be carried out in mice and rats. For some disease models, such as Parkinson's disease and epilepsy, rats are a more suitable model as the brain is larger, making targeting small areas easier. For other studies, such as tumour studies, generally mice will be used as. We expect the majority of animals to be used for safety, and tracking work in healthy animals, approximately 3500 mice and 600 rats over the 5 years license. Devices tested for safety is expected to use lower numbers, with 200 mice and 500 rats over the 5 year license. For the different disease models, the numbers will vary. Tumour modelling has a limit of 2600 mice and 400 rats over 5 years, Parkinson's disease has 500 mice and 1500 rats over 5 years, nerve injury has 1500 mice and 500 rats over 5 years, and epilepsy has 200 mice and 500 rats 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?

From our previous work, we don't expect the materials we use to have any particularly strong adverse effects. What we have discovered is that some animals after intravenous injection can have respiratory distress, which will be monitored closely in the minutes after injection. For the first part of the license, involved in testing materials in healthy animals, we expect most animals to experience minimal stress or discomfort, as they are often injected with materials once and then culled for sample collection. However, the protocol itself has the allowance for live imaging, repeated doses and blood sampling, so some animals

may have repeated handling. None of the steps in the non-disease models give more than transient distress or suffering, such as intravenous injection, or are carried out under anaesthesia. For the disease models, each has its own adverse effects and humane endpoints listed. The models which could have the greatest chance of adverse effects are the tumour and epilepsy models. For both models, adverse effects will be limited by having regular, thorough checks of the animals. Particularly for tumour-bearing animals, a checklist of adverse effects ranging from mild to severe will be used to assess welfare. For all models, adverse effects will be monitored and if animals are thought to exceed them, the NVS will be asked for advice, and animals will be culled if they reach humane endpoints. For all animals, at the end of the study they will be culled either by schedule 1 methods or by a procedure to collect samples. In the vast majority of cases, organs and/or blood will be collected for examination to maximise the information gained from each animal.

Application of the 3Rs

Replacement

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

Replacement

Due to the complex nature of the diseases we are investigating, it would not be possible to test the strategies we have without testing in animals. Before materials or devices are tested in animals, they will first be tested in cell cultures to check the safety and to help determine the best doses. In the initial stages, as we are interested in where the materials go and what they interact with in the body, it would not be suitable to use only cell culture methods. While it is possible to use 3D tumour models grown in culture, this does not give enough information on treatments which are administered through the bloodstream and their ability to target tumours, for example. For brain disorders such as Parkinson's disease and epilepsy, which are disorders of the whole brain, it is necessary to study the whole organ. As well as this, behavioural changes are an important measure of how effective a treatment is, which can only be done in animals.

Reduction

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

Reduction

The main way we will reduce the number of animals we use will be to use live imaging techniques. This will allow us to image the same animal over time instead of the more traditional method of culling a different animal at every timepoint to watch distribution of materials or to assess disease progression. Where materials are being tested for the first time in animals, pilot studies will be run with smaller numbers to ensure safety before starting larger studies. We will also meet with statisticians to gain advice from pilot studies to help design experiments with correct animal numbers. We will also endeavour to use randomisation and blinding which help to avoid bias wherever possible to increase the quality of data.

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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 most appropriate for the work being carried out as they have circulatory, nervous and excretory systems very similar to humans, which allows us to model where the materials go, how the body breaks them down and how they are removed from the body in a system similar to humans. There are also a range of techniques available in mice and rats such as imaging techniques, genetically altered strains and molecular biology methods which can maximise the information obtained from each animal. Using the most appropriate disease model will also help refinement, for example in Parkinson's disease we use a model which only gives symptoms in half the body, which reduces the stress on animals and doesn't interfere with their daily behaviour.