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	Anti-cancer therapy validation
Key Words	Cancer, Therapy, Biomarkers
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.

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

Despite significant advances in some areas, there remains a pressing need to develop new treatments for cancer. We aim to generate data for ~10 approaches that will enable an informed decision to be made as to whether they are suitable to progress into patients.

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)?

1. We will learn how new therapies work in models of cancer.

2. We will learn how we can monitor the effects of the therapies using approaches that can also be used in patients

3. We will be able to ensure that beneficial effects on tumours are not confounded by negative effects in other tissues that would affect quality of life in patients

We anticipate that as a result of this work, 1-3 new strategies will progress into clinical trial and that we will also have provided sufficient information to stop progression of therapies unlikely to be of benefit in patients.

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

The studies will use mice. We anticipate the use of 3300 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?

For the vast majority of studies, we will establish tumours within the animals. We may track how the tumours are developing using imaging approaches that can also be used in patients. Animals will be dosed with therapies, alone or in combination, at well tolerated doses using the route of least severity and the minimum number of doses to produce an anticipated anti-tumour effect. We will monitor closely how well the therapy is working and whether it is causing any side effects. We will not allow tumours to grow bigger than 1.25cm^3. Animals will then be humanely killed and tissues may be taken for further laboratory tests.

Application of the 3Rs

Replacement

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

Replacement

Where possible, we gain information of how the therapy might be working using cell lines and/or computer aided approaches. However we are not yet able to model in the laboratory everything that can happen within the whole animal (person) when a cancer therapy is given. This necessitates the use of animals. .

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Reduction

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

Reduction

1. We use as similar animals as possible to reduce inherent variability, improve experimental consistency and confidence in outcome findings.

2. We start treatments when tumours are the same size which offers a substantial reduction compared to starting all treatments on a designated day with tumours of variable size.

3. We focus on experimental design to ensure that we have the best chance of gaining consistent data that we are confident in, using the lowest number of animals

4. We frequently use imaging that allows us to make multiple measurements in the same animal

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

1. We use rigorous monitoring processes to ensure we minimise welfare costs to the animals. We have developed health score systems over many years that provide a more holistic overview of potential harms we are causing and how and when to intervene such that harms are minimised.

2. We consistently refine our surgery techniques to aid recovery and have introduced revisions to pain management to improve welfare.

3. We will use behavioural testing which allows us to identify early detrimental changes in brain function which can occur as a consequence of some cancer therapies and is of huge burden within cancer patients.