

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	Palatability studies on Veterinary Medicinal Test Formulations
Key Words	Palatability, veterinary, medicinal, drug, formulation, dog, cat.
Expected duration of the project	5 years

Purpose of the project (as in ASPA section 5C(3))

Purpose	
Yes/No	(a) basic research;
	(b) translational or applied research with one of the following aims:
Yes/No	(i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants;
Yes/No	(ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants;
Yes/No	(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.
Yes/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);

Yes/No	(d) protection of the natural environment in the interests of the health or welfare of man or animals;
Yes/No	(e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work;
Yes/No	(f) higher education or training for the acquisition, maintenance or improvement of vocational skills;
Yes/No	(g) forensic inquiries.

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

- The aim of the current project is to assess the palatability / level of acceptance of new dosage forms of existing veterinary medicinal products for oral administration to cats and dogs.
- For example, a liquid formulation of a tablet used to treat high blood pressure in cats has been developed and its palatability will be assessed in cats, to ensure that it is easier to administer to the cat than the tableted form. This will reduce stress in both the cat and its owner.
- The most palatable test formulations of each medication are selected for further product development.

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)?

A new palatable oral dosage formulation / medicine offers a more convenient dosage form for cats and dogs than a conventional tablet, reducing stress for both animal and owner during administration. If a liquid formulation, it allows the dose to be more accurately assigned to ensure the animal is on the lowest effective dose, which makes it a safer and more convenient treatment option.

This project will provide the formulation development team with palatability scores for new oral dosage test formulations of existing veterinary medicinal products. Based on this information, decisions will be taken regarding subsequent product development. This will ultimately provide confidence that the veterinary medicinal products developed will be readily accepted by the animals that they are administered to.

By ensuring that the most palatable oral dosage formulation of a veterinary medicinal product is brought to market, this project will increase animal acceptance of medication for a range of conditions in cats and dogs. Such benefits will be realised through increased confidence of veterinary surgeons in the products and an increase in the prescription rate. Furthermore, there is a particular benefit in those diseases that require daily lifelong treatment as acceptance of drugs in animals receiving daily treatment can decrease over time. It will also increase owner compliance as often administration of unaccepted drugs can be stressful for owners.

Palatability of a veterinary medicinal product is of clear benefit to the Veterinary Surgeon as it facilitates administration of the product and ensures treatment compliance. This leads to short, medium and long-term health benefits in the animal itself and a more positive experience for the owner.

It is likely that this project will identify the most palatable oral dosage formulations / medicines for veterinary medicinal product development.

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

During the five-year lifetime of the licence, we expect to use up to 500 cats and 500 dogs.

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?

During this project, new oral dosage formulations / medicines will be offered to cats and dogs, using different approaches such as:

- (i) in a clean dry bowl
- (ii) in a bowl on food
- (iii) via an oral dosage syringe into the oral cavity
- (iv) offered by hand

Observations during administration will be recorded based on:

- **level of acceptance** of the article e.g. full consumption, partial consumption, no consumption and/or
- **behaviour** of the animal e.g. grimace, lick, sniff and walk away.

As most of the test formulations will be oral dosage formulations of existing, conventional veterinary tablets, expected adverse events will be similar to the adverse events listed on the product labelling of the marketed tablets/products. The maximum expected level of severity of adverse effects that animals may experience is moderate and these will be short term.

The most common adverse effects that animals may experience during this project are listed below:

- Vomiting
- Transient diarrhoea
- Transient anorexia
- Transient lethargy
- Dehydration
- Mild gingivitis
- Hyperactivity, excitability
- Panting
- Elevated heart rate
- Elevated liver enzymes
- Decreased appetite
- Blood in faeces
- Excessive thirst
- Excessive urination
- Excessive hunger

If animals are deemed healthy by a Veterinary Surgeon at the end of the study, they may be re-used or re-homed.

Application of the 3Rs

Replacement

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

Replacement

The palatability / level of acceptance of a medicinal product by an animal is influenced by many factors such as texture, smell, taste, colour. Currently, there are no suitable non-animal models that reliably predict if a product will be palatable to the target species. As such, palatability of an oral test formulation / dosage form must be demonstrated in appropriate animal studies.

Reduction

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

Reduction

In the early stages of product development, the palatability of each oral dosage test formulation / medicine will be assessed in 5-10 animals. When a test formulation has been selected from the screening phase, or where only one formulation is available, its palatability is assessed in up to 20 animals. Selection of the appropriate study design ensures that the minimum number of animals is employed.

Adequate animal numbers and voluntary uptake should give a clear indication of palatability. Where smaller animal numbers are involved the use of a reference product can help minimise inter-animal variability.

Furthermore, animals will be selected based on health and eating behaviour to ensure selected animals represent normal feeding behaviour **i.e. no greedy or picky eaters.**

Following confirmation from a Veterinary Surgeon, animals that are not suffering or likely to suffer as a result of the procedures experienced during a palatability study may be kept alive pending re-use, under the care of a Veterinary Surgeon.

Animals will not be re-used if the actual severity experienced by the animal in any previous regulated procedure/series of regulated procedures was classified as 'severe'.

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 species employed for each palatability study must reflect the target species for the oral dosage test formulation / medicine being evaluated.

The following refinement controls will be applied to minimise welfare costs to the animals:

Administration of oral dosage test formulations / medicines

All personnel performing administration are trained and competent. They have been supervised by Veterinary Surgeons during their training to ensure they are aware of best practice.

If administration of test formulations results in or induces evidence of suffering in an animal that is greater than moderate or transient, the animal will be humanely killed unless, in the opinion of a Veterinary Surgeon, such complications can be remedied promptly and successfully using minor interventions (such as providing fluids, wet food, additional warmth or basic symptomatic veterinary treatments).

Monitoring

All animals are monitored by competent personnel at regular intervals after administration. Daily health monitoring is conducted throughout the period the animals are on study. This aims to detect potential adverse events early and prompt intervention should keep suffering and distress to a minimum. Adverse events will be investigated and treated by veterinary surgeons.

Humane endpoints

Animals will be euthanised if no improvement in condition is seen at the start of the third consecutive day of treatment, despite treatment as described above.

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	Next Generation of Delivery Systems for Pharmaceuticals
Key Words	Cancer, nucleic acids, biomaterials, chemotherapy, vaccines,
Expected duration of the project	5 years

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.
Yes	(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 project will use novel pharmaceutical delivery systems to improve the response to a range of drugs. These drugs will be used in a number of conditions including: cancer treatment, chronic wound healing, bone repair, vaccines and other therapeutic applications. This involves testing the therapeutics individually and in combination with other traditional therapies such as chemotherapy. Delivery systems will also be used with the drugs which are designed to reach the target tissue and cells. Therefore, this project licence is designed to test new delivery systems that could lead to safer, more effective treatments for a variety of diseases.

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 main benefits of this project include better treatment outcomes with fewer side effects for patients, improved vaccines, faster healing and tissue repair, and more accurate tools for detecting and monitoring diseases in both humans and animals. Within the lifetime of this licence, we expect to publish >25 research articles in respected scientific journals. These publications will share important findings about the safety and effectiveness of new medicine delivery methods for cancer treatment, immune therapy, and tissue regeneration. The research will also be presented at scientific conferences and may lead to review articles that help establish our laboratory as a leader in this field. These outputs will advance medical knowledge and provide essential data that other researchers and pharmaceutical companies can use to develop new treatments. In the longer term (5-10 years beyond this licence), the successful delivery methods and diagnostic technologies developed through this programme are expected to result in 3-5 patent applications. These patents will protect our new discoveries and form the basis for partnerships with pharmaceutical and biotechnology companies, licensing agreements, or new spin-out companies. The comprehensive safety and effectiveness data we generate will be essential for getting regulatory approval and moving towards human clinical trials. Ultimately, this pathway aims to bring innovative treatments and diagnostic tools to patients and veterinary clinics, improving health for both humans and animals while supporting the UK life sciences industry and economy. The anticipated results should generate significant commercial interest and a data package that will help with this process. All of these factors are essential if we are to develop healthcare products that can significantly impact upon patients that have no other treatment options. We also anticipate that our results will impact upon the scientific community, clinicians and government decision makers.

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

Normal or genetically modified mice and rats will be used within this project licence. Over a 5 year period would expect to use a total of 12,200 animals.

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?

All animals will be housed, normally in small groups, with continuous supply of fresh food/water as well as adequate space with appropriate environmental enrichment (e.g. nesting material).

Environmental conditions such as Light, ventilation and temperature are controlled and monitored to ensure appropriate conditions are maintained.

The majority of the protocols in the licence are classified as mild or moderate. We have over 25 years experience with both the therapeutics and the delivery systems that will be delivered. Any adverse effect is expected to be mild and typically, post-treatment, the animals drop ~5% weight for the first 24 h but regain their normal weight by 48 h. We do not predict any severe or even moderate adverse effects.

Some animals will be given tumours but we will not allow them to adversely impact the health of the animal. Some of these tumour models can grow quite fast and so the skin surrounding them can become irritated and thin, sometimes even necrotic. We will actively monitor this and use painkillers/antibiotics as required. Some tumour models, can develop ascites (a build up of fluid in the tummy) – this is also seen in patients. These models are used infrequently and we will ensure that if ascites is present, it does not impede normal behaviour and we will cull any mice a maximum of 7 days after ascites is noted to minimise any potential for severe adverse effects. Our aim is to treat early tumours (including metastases) before they reach a debilitating size. In these protocols, frequent monitoring will ensure that we can prevent significant consequences.

We will create small skin wounds on the backs of some animals and then treat them to improve healing. Wounds are dressed and pain relief given. Animals may experience mild pain or discomfort for the first 24–36 hours, but significant suffering is not expected. No infection is expected.

Small sections of cranium may be removed and treated with bone regenerating substances. Animals may experience moderate pain and discomfort in the immediate recovery period. This should not cause any severe problems and will be managed by giving painkillers post-operatively.

Mice will be given treatments various different ways often several times, in a similar way to how patients are treated; into the bloodstream, through the mouth or nose, injections into/under the skin, into the peritoneal cavity and/or directly into the tumour. Any injections are normally associated with very short-term discomfort. Mice will be given anaesthesia before and during any surgery, some of the injection procedures to deliver cells into the bloodstream and/or some treatment routes. Adverse side effects are minimal (approx. 1 in 200). Rigorously defined end points are explicitly stated throughout all protocols as agreed with the named veterinary surgeon. Any animal that is at risk from exceeding agreed endpoints in any protocol will be humanely killed to ensure animal suffering is kept to a minimum.

Application of the 3Rs

Replacement

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

Replacement

The objectives of this project are to test a range of delivery systems to improve the bioavailability of drugs for cancer, vaccines and regenerative therapies. No animal studies will commence without extensive testing in the laboratory. To progress new medicines along the development pipeline, it will be essential to determine the action of such drugs in a physiological environment. Before any studies in animals are carried out, we will use a wide range of non-animal models to gather information, including traditional cell cultures, three-dimensional cell clusters (spheroids), and miniature “lab on a chip” systems that mimic how tissues behave in the body. These approaches allow us to test and optimise our drug delivery systems in a controlled environment and reduce the number of animals needed. Despite this extensive use of replacement models, it is still necessary to study some drugs in animals, because only a living body can show how the treatment behaves in a complete, functioning system. These studies help us determine how effective the treatments are and their potential benefit to patients. Animal studies will only be undertaken only after thorough testing in non-animal systems. Studies are always designed to improve upon current medicines already used. Thus, the use of animals in this project is essential to enable us to determine the true potency of our drug loaded delivery devices and their potential clinical value. No other alternatives will create the physiological environment required for acquiring pre-clinical data. No animal experiments will take place unless absolutely necessary.

Reduction

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

Reduction

Any animal studies will only happen after extensive laboratory and computational studies are completed. We will ensure a clear and testable hypothesis is formulated before each individual experiment. We will use online resources such as the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3R)'s Experimental Design Assistant to ensure our experiments are properly designed to maximise robust, reproducible outputs and these are appropriately reported. We will seek feedback and advise on experimental plans from researchers locally as well as international colleagues.

In addition, small pilot studies will provide initial insights into the likely differences in response between treatment groups. This will facilitate the planning of adequately powered, larger-scale studies containing sufficient numbers of animals to uphold statistical significance, thus avoiding the need for unnecessary repetition. A detailed experimental plan will be submitted, reviewed and approved by an experienced panel who oversee *in vivo* studies in our facility before any individual study can start. This provides additional independent experienced oversight.

Finally, where feasible, we aim to archive relevant tissues from animals undergoing procedures to reduce numbers needed if we had a future scientific interest in examining tissues.

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

- All procedures described in this licence will observe good laboratory standards including appropriate use of pain relief when required, and all procedures will be carried out by trained and experienced personnel.
- All mice will be supplied with specialised nesting boxes allowing for animal shelter but also allowing for in cage animal health/welfare assessment.
- Pain relief will be given following surgery and /or some treatments to minimise suffering.
- Mice will be weighed, and overall appearance (body condition score) assessed at the beginning of experiments and 2-3 times a week thereafter to ensure they maintain a healthy weight and are not displaying signs of pain, illness etc. If changes are observed, frequency of monitoring will increase.
- The tumour models in the experiments have already been characterised in the past. We have had previous experience of these models and much of the toxicology and radiation work have been done previously
- Tumours (if any) will be measured 2-3 times a week (potentially more frequently as approaching limit) to ensure the tumour does not grow too large.
- For internal/metastatic tumours we will label the cells so these can be detected using non-invasive imaging
- For new treatments, we will first carry out small pilot studies to assess safety and efficacy and optimise the minimal effective dose for future studies

At all times the welfare of the animal is paramount, and experiments will be terminated at the first sign of suffering.

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	Production of Novel Monoclonal Antibodies for Therapeutic and Diagnostic Development
Key Words	Antibodies, therapeutics, diagnostics, immunotherapy
Expected duration of the project	5 years

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.
Yes	(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 aim of the project is to provide a service for the production of antibodies where these cannot be made by non-animal alternatives or these approaches have failed. Antibodies will be developed for the treatment or diagnosis of disease (such as cancer) or used for medical research. The methods employed will ensure that the antibodies produced will be of a high quality and suitable for the intended use.

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 project is likely to provide a wide range of potential therapy candidates for conditions with no existing effective treatment. Each successful immunisation will generate a panel of specific antibodies against the project target protein. These antibodies can be purified for use in disease detection and diagnosis in both humans and animals. In addition, promising antibodies can be further developed into potential therapies for disease treatment either by themselves (monoclonal antibody therapy) or by attaching a drug payload to the antibody to bring a drug into direct contact with a target cell (Antibody-Drug conjugation - ADC). ADCs can lead to toxic drugs being delivered to diseased cells more specifically, reducing toxicity to normal, healthy tissue. The project will also provide new antibody-based methods of detecting, predicting and monitoring diseases in humans and animals. New antibody tools for biological research expanding understanding of biological processes and disease mechanisms will be developed and produced for university laboratories and pharmaceutical and diagnostics companies both within the UK and internationally.

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

Over the course of 5 years, we expect to use up to 100 rabbits and 500 mice.

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 animals will undergo a maximum of 6 immunisations and up to 5 blood withdrawals over the course of the study (needle sticks). The expected severity is classified as moderate. The adverse effects are expected to be minimal with the possibility of minor irritation at the site of injection or blood withdrawal. In this case, animals will be monitored for signs of pain and weight loss, and, when necessary, may be given treatments and soft food.. If animals show adverse effects after immunisation that do not improve with treatments within 24 hours (painkillers and antimicrobials), or develop lesions that exceed the authorised severity without prior signs (large granulomas or ulceration), they will be humanely killed. However, based on our previous projects this is a rare occurrence. At the end of the study the animals 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

Antibodies are the product of an extremely complex immune response, occurring within animals. This process is too intricate to be replicated fully and exactly in vitro with current technology. Non-animal alternatives such as mammalian display (OptiMAL®), phage display (OptiPHAGE), *in-silico* affinity maturation (RAMP®) and AI/ML-ab (AI-driven) platforms and libraries are available which mimic certain aspects of this, and we will utilise these approaches in preference over rabbit B cell cloning or mouse hybridoma, following a strict decision process which emphasises a non-animal approach. However, in some cases these may not be suitable to fully replace animal-derived antibodies for all purposes.

Reduction

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

Reduction

The number of animals used will be the minimum number required to generate immune tissue for antibody generation: 2 rabbits and typically 3 mice (up to a maximum of 5). This number has been determined by experience gained during previous projects. We will continue to refine our techniques to identify means of reducing the number of animals used without compromising the antibodies produced.

Once the antibodies have been produced the techniques used mean that a continual supply can be made in vitro without the need for any further animals to be used.

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.

Mice are the lowest vertebrate group that can be used to make antibodies and our first choice of animal species for immunisation. Rabbits are used when mice are unsuitable because they produce antibodies that are very specific and are better for some applications such as therapeutic drug development. Rabbits produce greater diversity in the antibody repertoire. This can be particularly important if the target is too similar to the mouse equivalent protein. Complete records of the health screening and welfare observations will be maintained. The quality will be assessed via retrospective review. Animals will be closely monitored to ensure they are maintained with lowest grade harms possible as detailed in this licence. We ensured that all the procedures included in the protocol are the least harmful and stressful for the animals, such as subcutaneous inoculations (over intraperitoneally), TiterMax gold as adjuvant (over Freund's adjuvants), the use of numbing cream prior to injections (in rabbits), the use of playpens and human interaction (rabbits).

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	Diagnosis and Control of Endemic Diseases of Poultry
Key Words	Poultry, endemic disease, hatchery disease, enteric disease diagnosis
Expected duration of the project	5 years

Purpose of the project (as in ASPA section 5C(3))

Purpose	
No	(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):

The aims and objectives of this project are to produce virus isolates from diseased poultry samples in order to investigate the nature of these new and emerging viruses and their association with the disease. Viruses continuously evolve due to acquiring multiple random genetic mutations during their reproduction which they aren't able to correct leading to new and emerging strains. These strains can vary widely in pathogenicity meaning that birds may have little or no inherent immunity against new and emerging strains, resulting in greater disease burden to flocks. This genetic variability also means that existing diagnostic tests may fail to detect the new and emerging strains so that new or improved diagnostic tests may be necessary and could be developed as part of this project. A further aim of this project is to produce materials for diagnostic tests.

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)?

These viruses affect the health and growth of meat and layer chickens worldwide and have huge economic consequences, but their individual effects are largely unknown and require further investigation to develop diagnostic tests and control measures. This will vastly improve the health and growth of commercially farmed chickens.

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

Expected usage over a five-year period: chickens: 2300 and chicken eggs: 200

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?

Eggs and chicks will be inoculated with materials derived from clinical samples or with pure virus preparations to examine disease development. The effects of these viruses can be severe. In field infections they cause runting of embryos, which can be severe and greater than 50% of expected weight for age, and cause stunted growth (reduced weight gain) in chicks which can exceed 50% for the breed average in the first three weeks post hatch. As they are enteric viruses, in field infections they may result in diarrhoea and enteritis, which can be moderate to severe/ Also certain enteric viruses, especially pathogenic avian reovirus strains, can result in lameness, which can become severe. All animals will be humanely euthanised by a Schedule 1 method.

Application of the 3Rs

Replacement

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

Replacement

Unfortunately, many of these viruses do not grow in cell culture and chickens are their host species. It is not possible, at this time, to use non-animal-based methods to determine how severe diseases caused by these viruses are.

Reduction

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

Reduction

It is sometimes possible to adapt a virus to cell culture after it has been successfully grown in chickens which we always attempt to do, thereby reducing the numbers of chickens used to produce the virus in sufficient amounts for investigation. We also will use the minimum number of animals to produce results which are statistically valid.

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 viruses we are investigating naturally infect poultry and chickens are their main host species.
We usually infect day old chicks with a standard dose of virus or material preparation. We will add analgesic to reduce suffering and pain caused by the viruses. Chicks are monitored four times daily for clinical signs but if adverse effects are observed then monitoring will increase in frequency up to hourly for moderate levels of adversity. If we find the effects of the virus are severe on individual birds, and that humane endpoints are being reached, individual affected chicks will be humanely euthanised as soon as possible to minimise suffering.

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	In-Vivo Pre-Clinical Analysis of Novel Therapeutic Agents in the Treatment of Dermatological Diseases
Key Words	Mouse models, novel drugs, therapy, skin, hair loss
Expected duration of the project	5 years

Purpose of the project (as in ASPA section 5C(3))

Purpose	
No	(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.
Yes	(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):

This project aims to develop and validate mouse models of chronic skin conditions including vitiligo, alopecia areata, and chemotherapy-induced alopecia. These conditions affect a significant proportion of the global population and can cause considerable physical and psychological distress. Although treatments are available for some patients, responses are often incomplete and relapse is common after treatment cessation. Chemotherapy-induced alopecia affects up to 65% of cancer patients receiving systemic treatment and, while typically self-limiting, can become permanent in a proportion of patients — particularly those receiving taxane-based regimens — for whom no pharmacological prevention is currently approved. The in vivo models developed under this project will be used to test new treatments and to better understand how these diseases respond to targeted therapy, generating preclinical data to support the development of more effective therapeutic options for patients who do not respond adequately to existing treatments.

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)?

This project will provide reliable preclinical data to support the development of new treatments for vitiligo, alopecia areata, and chemotherapy-induced alopecia. These conditions can cause visible changes in appearance and significant emotional distress, and current treatments — where available — do not work for all patients and rarely achieve durable remission after treatment is stopped.

The project will produce validated mouse models that closely reflect the human disease process, alongside evidence on the safety and effectiveness of novel medicines, biologics, and topical preparations. It will also generate insight into the immune and cellular mechanisms driving these conditions, and how they change in response to therapeutic intervention.

In the short term, this work will help clients select the most promising treatment candidates and improve the design of future studies so that fewer animals are needed overall. In the longer term, it will support the development of more effective therapies and contribute to scientific knowledge in investigative dermatology, in alignment with the 3Rs principles of Replacement, Reduction, and Refinement.

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

This project will use mice, including both normal and genetically altered strains, at various life stages from newborn to adult depending on study needs. Across all protocols, we expect to use up to around 15,000 mice over five years. Around 5,000 will be used in breeding protocols, with the remainder in dose-finding studies or models of chronic skin disease such as alopecia areata, chemotherapy-induced hair loss and vitiligo.

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?

Animals in breeding protocols may experience mild to moderate effects associated with their genotype, depending on the line used. In models where coat changes or patchy hair loss occur as a consequence of the genotype, these are typically cosmetic and do not carry significant welfare impact. Animals that develop progressive hair loss with skin changes may experience moderate discomfort; these animals are managed under a moderate severity breeding protocol with specific humane endpoints applied before suffering becomes unacceptable.

In disease induction models, animals may develop hair loss, skin changes, or depigmentation. In the alopecia areata skin graft model, animals may experience post-surgical discomfort and localised wound inflammation during the recovery period, and a proportion will develop progressive alopecia following successful disease transfer. In chemotherapy-induced models, animals may experience mild to moderate systemic effects from the chemotherapeutic agent used, including transient weight loss and reduced activity, which are managed with analgesics and supportive care. In vitiligo models, topical application of the depigmenting agent may cause localised skin irritation in a small proportion of animals.

All animals are monitored at minimum once daily, increasing to twice or three times daily if any adverse signs are observed. Pain relief, soft bedding, easily accessible food and water, and appropriate enrichment are provided throughout. Humane endpoints are defined in advance and applied by trained personal licence holders without delay when reached. No animal will be permitted to experience uncontrolled or unrelieved suffering. At the end of all protocols, animals are killed using approved Schedule 1 methods.

Application of the 3Rs

Replacement

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

Replacement

We use many non-animal models in our skin disease research, including cell cultures, hair follicle cultures, co-culture systems, and advanced three-dimensional models such as skin equivalents, spheroids, and organoids. We also work closely with QIMA Monasterium, a leading non-animal research organisation, to ensure these approaches are used wherever scientifically valid before any in vivo studies are considered.

However, current non-animal methods cannot fully reproduce the complexity of living skin and whole-body disease processes. Conditions such as vitiligo, alopecia areata, and chemotherapy-induced alopecia involve interactions between skin, hair follicles, immune cells, circulation, and other organs that can only be studied accurately in a living organism. These models cannot fully capture treatment absorption, distribution, metabolism, systemic immune responses, or side effects in other tissues.

For alopecia areata, an intact immune system is needed to model the autoimmune attack on hair follicles and the systemic immune response. For chemotherapy-induced alopecia, whole body regulation of the hair cycle and drug pharmacokinetics are essential. For vitiligo, systemic T cell priming, activation, and trafficking to the skin must be studied. As these processes cannot yet be fully replicated in vitro, some animal models remaining necessary. These are only undertaken after non-animal data has been generated and reviewed, and only where there is a clear scientific justification.

Reduction

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

Reduction

Studies will be carefully designed and appropriately powered to ensure that only the minimum number of animals necessary to achieve scientifically robust results are used, thereby avoiding unnecessary repetition. Sample sizes will be determined using power calculations informed by published literature and pilot data generated at the establishment or provided by QIMA Monasterium from their existing experience with equivalent models. This cross-group collaboration will help reduce the number of pilot animals required by drawing on existing knowledge and comparable datasets. Further advice on experimental design and analysis will be sought, where needed, from resources such as PREPARE (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence) guidelines and the NC3Rs (National Centre for the Replacement, Refinement and Reduction of Animals in Research) experimental design assistant tool.

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 main dermatology models used in this project rely on non-surgical methods such as topical treatment, immune activation, cell transfer, or administration of medicines affecting hair growth. These approaches have the lowest welfare impact because they do not involve major surgery, any adverse effects are visible on the skin surface, allowing close monitoring and early intervention. Whenever possible, these less invasive methods are preferred.

Some studies require more complex models, such as skin grafting or antibody transfer, to investigate conditions like alopecia areata or vitiligo. These procedures carry higher welfare risks, including local wounds or immune reactions, so animals are given pain relief, soft bedding, and enhanced monitoring during recovery. Non-surgical methods such as imaging and minimally invasive sampling are used whenever possible to reduce burden.

Non-invasive or minimally invasive assessments, including photography, skin scoring, in vivo imaging, and transepidermal water loss measurement, are used in place of more frequent tissue collection where possible. Non-invasive methods can still cause some degree of discomfort, where this is observed methods will be adjusted and welfare reviewed.

Less sentient species are not suitable for these studies as they cannot replicate the structure, hair biology, immune responses, or whole-body interactions of mammalian skin required for diseases such as alopecia areata and vitiligo. The establishment will work closely with QIMA Monasterium throughout the project so that findings from in vivo studies can be followed up in human tissue-based non-animal systems, wherever scientifically possible, helping to reduce further animal use.

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	Safety and Efficacy of Veterinary Medicinal Products in Domestic Species
Key Words	Safety and efficacy
Expected duration of the project	5 years

Purpose of the project (as in ASPA section 5C(3))

Purpose	
No	(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;
Yes	(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.
Yes	(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):

To fulfil regulatory requirements with regards to the safety and efficacy of new veterinary medicinal products in the target species. The safety of these products for consumers of food producing animals will also be investigated.

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 potential benefits that will be derived from this project include the development of new veterinary medicinal products that are:

- (i) safe and effective for treatment of companion and food producing animals
- (ii) authorised for marketing in the United States and the rest of the world
- (iii) available to the end-user for treatment of a wide range of illnesses/diseases
- (iv) safe for use in food producing animals.

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

Approximate animal requirements for the five-year lifetime of the licence are presented in the following table:

Species	Number
Cattle	500
Sheep	100
Pigs	100
Goats	100
Horses	100
Dogs	80
Cats	100

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?

Veterinary surgeons will determine if animals are suitable for a study by clinical examination and analysis of blood tests. Selected animals will be treated with test and/or reference veterinary medicinal products, and the levels will be measured in sequential blood samples to determine the safety / efficacy profile of each product.

Animals will be restrained, which may cause short periods of stress, and the product will be administered either orally, topically, or by injection, which will cause short term-pain. Furthermore, multiple blood samples will be taken by insertion of a needle into a vein, which will also cause short-term pain.

In a small number of studies, it may be necessary to individually house animals in accordance with regulatory requirements, however this will be for the minimum period necessary to achieve valid scientific outcomes.

When an animal is moved into the facility, an acclimatisation period of no less than 7 days will be necessary to allow the animal to adapt to its surroundings, and to help reduce any stress caused by the experience.

Expected adverse effects vary according to the test/reference product administered. They include vomiting, diarrhoea, lethargy, dehydration and inappetence. With certain products animals may also experience effects such as skin infections, dermatitis, swollen lymph nodes, reduced heart rate, hypothermia and cystitis. There may also be some bruising, swelling and pain at injection sites which will be kept to a minimum by best practice. The expected level of severity of such adverse effects is moderate. However, severity will be controlled by daily monitoring of animals on study to ensure prompt intervention to keep suffering and distress to a minimum. Where necessary, treatment will consist of cessation of administration and additional intervention as recommended by the veterinary surgeon. If an animal does not improve in spite of treatment or the condition rapidly worsens, the animal will be humanely killed.

Adverse effects associated with blood sampling or catheterisation sites include inflammation of the surrounding skin or inflammation of the catheterised vein. There may also be bruising of the skin surrounding the site. Best practice will ensure these are kept to a minimum and twice daily monitoring will be conducted to identify any issues as early as possible.

On completion of the study, animals may be rehomed (all species), sent for commercial slaughter (farm species) or re-used (all species) as deemed appropriate by the Named Veterinary Surgeon (NVS).

Application of the 3Rs

Replacement

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

Replacement

Regulatory guidelines require that specific criteria are proven in the relevant animal species, therefore the use of animal studies is unavoidable.

Where possible, veterinary medicinal products will be assessed using laboratory-based techniques to demonstrate equivalence between test and reference products, thereby avoiding the need for animal work, however such laboratory techniques do not always reflect how the products perform in animals. Nonetheless, laboratory-based methods will always be considered as an alternative to using animals in studies.

Reduction

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

Reduction

All new veterinary medicinal products will be tested using laboratory-based techniques to confirm as far as possible that design requirements have been met before proceeding to safety and efficacy studies in animals. This minimises unnecessary animal testing.

A full literature review will be conducted for each project to ensure that the findings of previous studies are accounted for during product design and clinical study design, which will in turn reduce unnecessary animal testing.

Early probe studies will be conducted using the minimum number of animals required to allow sound statistical predictions. The results of these studies will be used to optimise study design and limit the number of animals required to generate valid scientific outcomes.

Blank blood/plasma is harvested from animals and banked for subsequent development of laboratory test methods and control samples. This reduces overall requirements for negative control animals.

Overall, the number of studies to be conducted will be kept to the minimum required to permit the approval of each product on the market.

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

Each study will be designed to evaluate the new veterinary medicinal product in the target species in accordance with regulatory requirements, whilst minimising the number of blood samples required from each animal.

All housing provided will meet the standards of care and accommodation required by the Animals (Scientific) Procedures Act 1986. Appropriate species-specific enrichment will be provided:

- Dogs and cats will have toys to play with, the radio to listen to, handler interaction and social group interaction. They will have outdoor exercise areas with ramps, obstacles, hiding boxes & tunnels. Dogs will enjoy the use of a paddling pool and sandpit, while cats will have scratch posts, ladders, jumping platforms and an exercise wheel.
- Cattle will be provided with brushes, straw bedding and social group interaction.
- Pigs will be provided with mirrors, straw bedding, toys and social group interaction.
- Goats and sheep will be provided with straw bedding and social group interaction, while goats will also have access to a climbing frame.
- Horses will be provided with straw bedding and social interaction with other horses. They will be groomed and handled regularly.

Periods of individual housing will be kept to a minimum.

Animals will be monitored throughout the study by trained personnel, with a veterinary team available to advise on any additional care required.

Indwelling intravenous catheters can be used to facilitate blood sampling and reduce animal stress where multiple samples are required. These can be placed under anaesthesia to minimise stress to the animal.

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	Defining and Targeting Enzymatic and Signalling Pathways in Diabetic Retinopathy
Key Words	Imaging, Retina, Blood vessels, Diabetes, Polyamine pathway
Expected duration of the project	5 years

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.
Yes	(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):

Diabetic retinopathy is a diabetes-related eye disease and one of the main causes of sight loss in the United Kingdom and other developed countries. Current treatments do not work for everyone and are usually used only after the disease has already caused retinal damage and vision loss. Our recent research has identified a biochemical pathway that produces a harmful molecule called acrolein. Acrolein is also found in smoke from fires and pollution, but it can also be produced naturally within the body. In diabetes, this harmful molecule appears to build up in the retina, where it may damage nerve cells, support cells and blood vessels, contributing to disease progression. In this project, we aim to understand how acrolein affects different types of cells in the retina, including the blood vessels that become damaged and leaky in diabetes. We will also test potential treatments, including genetic approaches and new drug candidates, to find out whether they can slow, prevent or reduce diabetic retinal damage. If successful, this work could support the development of new treatments for future human clinical trials.

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-to-medium term, this project is expected to improve understanding of how diabetic eye disease develops and identify potential new approaches for preventing or slowing its progression. We will investigate whether acrolein, a highly reactive chemical produced within cells, contributes to damage to the light-sensitive and blood-vessel cells of the retina during diabetes. We will use genetic approaches to switch off proteins involved in acrolein production. This will help us determine whether blocking this pathway protects the retina and will provide evidence about whether drugs targeting the same pathway could be developed as future treatments. The immediate beneficiaries will be researchers working on diabetes and eye disease, who will gain new knowledge about the biological processes involved and potential treatment targets. In the longer term, if the findings support further drug development, this research could contribute to treatments that act earlier in diabetic eye disease, before irreversible sight loss occurs. This could ultimately benefit people with diabetes by helping to preserve vision and quality of life. Findings will be shared through scientific publications and presentations so that other researchers and clinicians can build upon the work.

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

We expect to use approximately 760 mice per year 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?

Genetically altered mice will be bred and maintained. The genetic changes are not expected to cause harm, based on our previous experience. Taking a small ear sample for identification and genetic testing may cause brief, mild discomfort.

Some mice will receive injections or eye drops to activate a genetic change. Restraint and administration may cause brief stress or discomfort, while the drug used may temporarily reduce food intake, body weight or activity. Eye drops may cause temporary irritation. Animals will be monitored during treatment and for several days afterwards, and further administration will be withheld if adverse effects develop.

Type 1 diabetes will be induced in some mice using repeated injections of a drug that reduces insulin production. The injections may cause temporary pain. Diabetes may cause weight loss, increased drinking and urination, dehydration, reduced activity and deterioration in general condition for several months. Most animals are expected to experience moderate harms, although some long-term studies are classified as severe because of the duration and cumulative effects of diabetes and other procedures.

Diabetic animals will be checked daily and weighed at least twice weekly. Monitoring will be increased if their condition deteriorates. Softened food, fluids or insulin will be provided according to defined criteria, and bedding will be changed as required to keep animals dry.

Other procedures may include administration of treatments or tracers, visual testing, retinal imaging and measurement of retinal function. These may cause brief restraint-related stress, injection-site discomfort or temporary eye irritation. Injections into the eye and retinal assessments will be performed under general anaesthesia. Breathing, body temperature and recovery will be closely monitored.

Animals will be killed humanely if they reach defined limits for weight loss, body condition or dehydration, cannot eat, drink or move normally, show substantial pain or illness, or develop persistent eye irritation.

Application of the 3Rs

Replacement

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

Replacement

We use cultured cells wherever possible to study biochemical pathways and molecular interactions. These cell-based systems help us understand how harmful molecules affect retinal cells and allow us to screen potential treatments before animal studies are considered. However, diabetic eye disease is complex and develops slowly over time. It involves interactions between nerve cells, support cells, blood vessels, immune cells and whole-body diabetic changes. At present, this cannot be faithfully reproduced using cell culture, isolated tissues or other non-animal alternatives. Animal studies are therefore needed to understand how the disease develops in the living eye and to test whether treatments can protect retinal structure and function.

Reduction

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

Reduction

For all experiments, statistical calculations will be used to ensure that the minimum number of animals is used while still producing reliable results. Wherever possible, tissues from animals that have undergone *in vivo* or behavioural studies will also be collected for molecular, cellular and functional analysis. This will maximise the information gained from each animal and reduce the need for separate groups. Controlled breeding strategies will also be used to minimise the number of animals that are bred but cannot be used in experiments.

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

Diabetic mice are widely accepted and extensively used as a model of human diabetic retinopathy. This model allows us to study early diabetic changes in the retina before severe sight loss occurs. Non-invasive visual testing and retinal imaging will allow changes to be followed without causing anything but mild discomfort. Where possible, compatible measurements will be combined during one period of anaesthesia to reduce the number of anaesthetic events. Animals will be kept warm during anaesthesia, and eye lubricant will be used to prevent the surface of the eye from drying. Diabetic animals will be checked daily and weighed at least twice weekly so that deterioration can be identified early. During diabetes induction, sugar solution will be provided to reduce the risk of excessively low blood sugar. Bedding will be changed every day to keep diabetic animals dry and comfortable despite increased urination. Defined changes in weight, hydration or blood-glucose levels will trigger increased monitoring and the provision of softened palatable food, fluids or insulin. When administering drugs or experimental treatments, minimum practical volumes will be used, and further treatment will be withheld if adverse effects develop.

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	Nutritional and Management Interventions to Reduce Environmental Footprint and Support Health of Pigs and Sows
Key Words	Pig, sow, nutrition, health, nutrient, environment, management
Expected duration of the project	5 years

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;
Yes	(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.

Yes	(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);
Yes	(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 current project licence has the ultimate goal of contributing to the reduction of pig farms' environmental footprint and enhancing animals' health and welfare, all without reducing production efficiency. Specific objectives are:

Obj. 1) To improve inputs and outputs efficiency (i.e., macro and micro nutrients, water, etc.) of pig systems

Obj. 2) To identify nutritional strategies (i.e., diet formulations, novel/circular/alternative ingredients) to reduce nutrient excretion and emissions without impairing animal health and productivity

Obj. 3) Support and enhance pig health and welfare in commercial conditions through nutritional and management interventions as opposed to antimicrobials

Background to the project:

Pig and poultry meat have relatively low greenhouse gas emissions per kilogram, but they are eaten in large amounts in the United Kingdom (UK) and Ireland, so they still have a significant environmental impact. In Northern Ireland, much of the nitrogen (N) and phosphorus (P) used in farming is imported through feed and fertilisers, which can upset the natural nutrient balance. Pig farming produces manure rich in N and P, contributing to problems like water pollution (eutrophication) and soil acidification. Reducing the environmental impact of pig farming is essential both globally and locally. The UK has set a target to cut carbon emissions by 68% by 2030, and agriculture—especially livestock farming—accounts for a notable share of emissions. Northern Ireland has also introduced climate laws that require farmers to lower their carbon footprint and reduce pollution such as ammonia emissions, which harm ecosystems.

One of the biggest environmental impacts in pig production comes from feed, which can account for up to 85% of total greenhouse gas emissions. Therefore, improving feed strategies and adopting more sustainable, circular approaches could help reduce carbon emissions, as well as N and P pollution, making pig farming more environmentally friendly and sustainable in the future.

Moreover, keeping pigs healthy is essential for sustainable and efficient farming. Poor health—whether caused by injuries (like lameness or wounds) or diseases (bacterial, viral, or other)—can slow growth, increase deaths, reduce animal welfare, and raise production costs. Treating these issues often requires antibiotics and other chemicals, which contributes to antimicrobial resistance, a growing global concern. Even mild or hidden diseases can still reduce productivity and, in some cases, pose risks to human health (such as Salmonella). Because of these challenges and the need to reduce antibiotic use, improving feed and housing management is important to prevent disease and support pig health.

This project focuses on identifying the most effective and affordable ways to improve both animal health and welfare, and to reduce the environmental footprint of pig systems.

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)?

This project focuses on improving pig farming in Northern Ireland and the UK so it becomes more environmentally friendly, efficient, and supportive of animal health and welfare.

Researchers will study how changes in pig diets and farm management can reduce pollution (such as carbon emissions, ammonia, and nutrient waste like nitrogen and phosphorus), while also improving animal welfare and reducing the need for antibiotics. They will also explore new, more sustainable feed ingredients, including locally produced or recycled alternatives to imported crops like soya.

The findings will be shared widely with farmers, advisors, policymakers, and scientists through reports, articles, conferences, and workshops. This will help farmers gradually adopt better practices on their farms.

In the short term, the project will provide practical recommendations, such as guidance on using new sustainable feed ingredients and/or implementing new management routines. Over the longer term, it aims to identify bigger improvements, like developing new feed sources and improving overall farm efficiency.

Overall, the project aims to help the pig industry:

- Reduce its environmental impact
- Improve animal health and welfare
- Increase farm productivity and efficiency

It will also strengthen scientific research, create new collaborations, and support future training and innovation in the field.

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

Pigs will be the only species used. It is estimated that approximately 10,400 animals will be used across all studies conducted over a 5 year period; albeit not all the animals will undergo regulated procedures.

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?

Most of the procedures/steps are mild, only four steps are moderate, and none are severe. Therefore, the majority of pigs might experience transient distress (e.g., due to handling, milk/faecal sampling or recovery from sedation), frustration (e.g., due to individual housing), and/or local pain and inflammation (e.g., due to blood sampling) as the most probable harms. The vast majority of animals will be sent to the slaughterhouse at the end of the study as they will be fit and safe for human consumption.

Application of the 3Rs

Replacement

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

Replacement

For all objectives the studies must be conducted on the live animal since the main effects of treatment will be on the health and/or behaviour, and performance of the animal. Currently there is no alternative means to test for animal responses such as performance and behaviour using a non-animal model. Moreover, biological variability observed in commercial conditions cannot be replicated in *in vitro* processes.

For nutritive quality of feed and environmental impact, the use of *in vitro* techniques and rapid non-destructive methods have been considered but while they can complement *in vivo* studies (contributing to a reduction in the number of animals/studies needed), they are not able to replace the need for animal studies results completely.

Reduction

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

Reduction

For all areas, a statistician will be consulted to determine the minimum replication required to account for natural variation and attain a statically robust result. Past experience within our group and evidence from scientific literature will also be consulted. The number of animals required will be further reduced through the use of appropriate experimental design.

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

Pigs will be the species used for this project as it aims to produce outputs relevant to commercial pigs and commercial intensive pig producers/farms. As an important aspect of this project is nutritional (including study of alternative protein sources and feedstuffs) and environmental research, the use of small enclosures where pigs are housed on their own (to allow the pig to assess individual food protein sources and properly separate urine and faeces) and metabolic chambers (that allow to measure gas emissions) are required for specific trials. Nonetheless, the level of animal suffering will be no more than that experienced under normal commercial conditions for the vast majority of the experimentation. Where animals are segregated for a specific experimental protocol, for example determination of digestibility or gas emissions, they will be monitored regularly and will always have sight, smell and sound of others. In all situation, animals will have environmental enrichment such as ropes and/or plastic toys.