Animals (Scientific Procedures) Act 1986

Non-technical summaries for project licences granted during 2015

Volume 31

Projects with a primary purpose of: Translational and Applied Research – Diagnosis of Diseases

Project Titles and keywords

1. **Development of tools to prevent and control avian mycobacteriosis in birds**
    - Avian mycobacteriosis vaccine diagnosis

2. **Testing Veterinary Vaccines for Quality, Safety and Efficacy**
    - veterinary, vaccines, regulation, quality, safety

3. **Embryonated Eggs for Diagnosis and Research**
    - Egg, Virus, Vaccine

4. **Infectivity and strain behaviour of prions**
    - infectious disease, BSE, scrapie, prion

Project 1	**Development of tools to prevent and control avian mycobacteriosis in birds**	
Key Words (max. 5 words)	Avian mycobacteriosis vaccine diagnosis	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
	X	Translational and applied research
		Regulatory use and routine production
	X	Protection of the natural environment in the interests of the health or welfare of humans or animals
	X	Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	To develop a vaccine and diagnostic assays to control avian mycobacteriosis in birds as the disease affects captive breeding programmes and some species recovery programmes in the wild. Diagnostic assays could be used to investigate epidemiology of the disease in wild populations. Other disease control measures involve the above and a range of environmental management options such as the use of reedbed treatment systems for removing bacteria.	
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)?	An efficacious vaccine and sensitive and specific diagnostic assays to identify infectious individuals would help control avian mycobacteriosis, and reduce onward risks by reducing environmental contamination. Understanding epidemiology of the disease in the wild helps conservation managers reduce risks and manage any negative impacts.	
What species and approximate numbers of animals do you expect to use over what period of time?	A maximum of 4000 birds may be either vaccinated or screened for disease over a five year period.	
In the context of what you propose to do to the animals, what are the expected adverse	Vaccination and taking a small blood sample are considered to be relatively mild procedures and animals will be released back into their previous	

effects and the likely/expected level of severity? What will happen to the animals at the end?	place of habitation once the vaccination or blood sampling is complete.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The current vaccine under investigation has been found to provide some protection i.e. reduced mortality from the disease so it could be considered that it is in the bird's best interest to be vaccinated. The diagnostic assay relies on blood parameters to elucidate disease status so cannot be replaced as such.
2. Reduction Explain how you will assure the use of minimum numbers of animals	As vaccination and diagnosis of disease may be beneficial to the bird, reducing numbers may not be desirable. For any investigations, appropriate sample sizes will be determined to ensure appropriate statistical power (but may not be limited to that, given the previous statement).
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	The procedures of vaccination and taking small blood samples have been honed over time and are considered to be of mild severity. Staff training and many decades of experience have honed bird trapping techniques to minimise welfare concerns for this work.

Project 2	**Testing Veterinary Vaccines for Quality, Safety and Efficacy**	
Key Words (max. 5 words)	veterinary, vaccines, regulation, quality, safety	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	X	Basic research
	X	Translational and applied research
	X	Regulatory use and routine production
	X	Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	The overall aim of this project is to contribute to control measures against important veterinary diseases by protecting animals through vaccination. To achieve this we need safe, potent, efficacious and stable vaccines. The tests required are regulatory requirements. Our objectives are to monitor the safety, potency, efficacy and stability of current and new vaccines, identify new vaccine candidates and use the information gathered to improve vaccination campaigns and knowledge about important veterinary 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)?	Immunisation of animals with high quality vaccines is the primary means of control for many animal diseases. This project will ensure that there is a supply of safe, potent and effective vaccines which is essential for the maintenance of animal health. Improving animal health also has a knock on effect on human health and economic prosperity. This project will also provide materials to research groups to enhance research activities into the infectious processes and immune responses associated with these animal diseases to improve our	

	knowledge and understanding and work towards tests that can be carried out without the use of animals in the future.
What species and approximate numbers of animals do you expect to use over what period of time?	Guinea Pigs - 850 Cattle - 985 Pigs - 450 Sheep and Goats - 300 Project expected to run for 5 years
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	Some of the regulatory requirements for vaccine manufacture do require the use of unvaccinated, control animals which will develop clinical signs of disease resulting in a severe limit for some protocols; however many animals will show none or miLd clinical signs.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	The testing of vaccines requires the host species to be used under regulatory and licencing authorities. However, prior to animal testing, vaccine strains are screened using cell culture techniques to help match them to field viruses against which protection is sought and to check that they have growth and stability characteristics suitable for vaccine manufacture and storage. Research is ongoing to develop improved methods to evaluate vaccine performance in the field, reducing reliance on the use of experimental animals; some of the work from this project will generate data that can be used in models already developed to assist with their validation.
2. Reduction Explain how you will assure the use of minimum numbers of animals	There is a minimum requirement for some of the mandatory testing required for licencing these vaccines so there is a requirement to use a certain number of animals for some of the studies. We are aiming to use the minimum required for each test.

3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Guinea pigs are being used to reduce the number of large animals being used as they are a suitable small animal model to identify new vaccine candidates for some of the animal diseases and for some of the regulatory safety testing. We have very strict humane end points and very well trained staff to prevent unnecessary suffering. For safety and potency testing of these veterinary vaccines the target species for the products have to be used. To minimise suffering we will carry out preliminary studies on the safety and efficacy of the vaccine being used in the challenge experiments to minimise the number of animals developing clinical signs. We can also use medicines under direction of the on call veterinary surgeon to reduce clinical symptoms.

Project 3	**Embryonated Eggs for Diagnosis and Research**	
Key Words (max. 5 words)	Egg, Virus, Vaccine	
Expected duration of the project (yrs)	5 years	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)		Basic research
	X	Translational and applied research
	X	Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
		Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	The project will provide support to work to diagnose, monitor and study viruses causing human infections.	
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)?	Influenza epidemics are associated with high levels of illness and death. Diagnosis of influenza infection provides a public health benefit by providing information on the number of virus infections in the population. This data can also be used to inform how well matched the vaccine is to the virus infecting the population and also how well the vaccine is performing in protecting the population.	
What species and approximate numbers of animals do you expect to use over what period of time?	Embryonated hen's eggs 500 eggs per year Five years project duration	
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	The likely severity is Mild. Expected adverse effects are from microbial contamination during the procedures. This is minimised by ensuring sterility of equipment, careful monitoring of the procedures and staff training. The embryos are terminated at the end of the procedure and before hatching.	

Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	Some viruses will only grow in embryonated eggs. Some diagnostic tests require high concentrations or volumes of virus which can only be achieved by growth in embryonated eggs. The majority of influenza vaccine viruses are produced in eggs. Diagnostic testing associated with the influenza vaccine must use egg grown viruses to preserve the characteristics of the vaccine virus.
2. Reduction Explain how you will assure the use of minimum numbers of animals	Wherever possible, mammalian tissue culture cells are used instead of embryonated eggs. When eggs are used the number of eggs is carefully selected to ensure that the aim of the experiment is achieved without unnecessary wastage.
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Use of eggs is restricted to purposes where they provide a significant benefit which cannot be achieved by the use of mammalian tissue culture cells. Training and sharing of protocols with other laboratories ensures that methods are updated and refined to achieve the best result. Careful husbandry is practised to ensure minimum wastage of eggs.

Project 4	**Infectivity and strain behaviour of prions**	
Key Words (max. 5 words)	infectious disease, BSE, scrapie, prion	
Expected duration of the project (yrs)	5	
Purpose of the project as in ASPA section 5C(3) (Mark all boxes that apply)	x	Basic research
	x	Translational and applied research
		Regulatory use and routine production
		Protection of the natural environment in the interests of the health or welfare of humans or animals
		Preservation of species
		Higher education or training
		Forensic enquiries
	x	Maintenance of colonies of genetically altered animals
Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)	The aim of this project is to evaluate the transmission properties and identify the strains of Transmissible Spongiform Encephalopathies (TSEs), which include Bovine Spongiform Encephalopathy (BSE) or mad cow disease. Key objectives are i) to complement surveillance for these diseases so novel TSEs that may have potential to infect people are identified and policy making bodies are informed ii) provide information on TSE strains and how they may involve when they transmit from animal to animal and if they can acquire transmissibility to man, iii) study the distribution of prions in peripheral tissues and iv) investigate how prions may be released and how viable they are in the environment.	
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 results of this research have a number of potential benefits to an improved understanding of disease processes and the causative organisms. A key benefit is to continue safeguarding public health and animal welfare from a new BSE-like outbreak. The challenge currently is not identification of the BSE as it is traditionally known. The challenge lies in the recognition of i) new TSE strains that have the potential to evolve to BSE or ii) strains derived from BSE which, except animals, can also infect man. To achieve this objective an in depth knowledge of prion biology prion strains and their ability to evolve is	

	required. Also, research under this project will further increase our knowledge regarding how prions shed in the environment, how they enter in animals, how they multiply in them and ultimately how they cause disease. This will have a direct impact in safeguarding animal health and welfare, and public health.
What species and approximate numbers of animals do you expect to use over what period of time?	Transgenic mice Up to 4000 mice may be inoculated with TSE over the 5 year duration of the licence. Up to 3000 mice may be bred but not challenged with BSE as a result of breeding.
In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?	The majority of animals will be challenged with a TSE. This is achieved by deposition in the brain of a small amount of potentially infectious solution under general anaesthesia. Adverse effects from anaesthesia such as prolonged recovery times or ataxia or convulsions are very rare are extremely unlikely. Intra-cranial injections can in rare cases cause unpredictable sudden death, pain seizures, lethargy, hypoactivity, depression, anorexia, weight loss, social isolation, aggression and wound scratching/swelling. These adverse effects are very rare due to the high clinical and surgical standards applied. However, when they occur they are recognised promptly and affected animals are euthanized, however as unpredictable sudden death occurs in a very small proportion. The majority of challenged mice will develop TSE, which can result in waddling gate, poor body condition and weight loss, hyper- or hypoactivity, rough coat, hunched back. These symptoms are promptly recognised by experienced staff who receive rigorous training and the animals are euthanized before their condition reaches a severe limit. Consequently animals are not expected to experience more than moderate severity.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot	It is impossible to eliminate animal experimentation from prion studies. This is because prions are believed to consist only from proteins. So, unlike bacteria or viruses, no reliable molecular or cellular

use non-animal alternatives	biological methods can be used to analyse them. Therefore, animal experimentation is an unavoidable consequence. However, *in vitro* methods for prion detection and strain recognition are being developed. Under this licence these new tests will be assessed as they arise.
2. Reduction Explain how you will assure the use of minimum numbers of animals	Every, effort is made to keep animal use to a minimum (use of transgenic mouse lines with higher sensitivity and specificity to TSEs, application of appropriate statistics to calculate minimum number of animals per study).
3. Refinement Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.	Every effort is made to refine all experimental procedures and maximise animal welfare. To achieve this animals are checked daily and environmental factors such as ambient temperature are kept at optimal levels. Mice are social animals so they are housed in groups as part of their social enrichment. Further environmental enrichment is offered and regularly reviewed to ensure the best possible housing. This includes appropriate bedding introduction of small items to keep the animals interested. As onset of clinical TSE differs in individual animals in some cages single mice may be housed for a period of time. To minimize the impact of single housing a female cage mate (such as ex-breeders or surplus stock) is introduced to singly housed females with notable success. This cannot be applied to male animals as they tend to fight. Staff are trained rigorously in the recognition of clinical signs of TSE and every six months their competence is assessed so they recognise the disease at early stages before it causes severe discomfort.