Animals (Scientific Procedures) Act 1986

Non-technical summaries for projects granted during 2014

Volume 26

Projects with a primary purpose of: Higher education or training for the acquisition, maintenance or improvement of vocational skills

Project title and keywords

1. **Pharmacology for MSc Students**
   - Education, Respiration, Renal, Cardiovascular, Pharmacology

2. **Education in pharmacology**
   - Education, Pharmacology, Cardiovascular, Respiration, Renal

<table>
<tr><td>Project 1</td><td colspan="3">Pharmacology for MSc Students</td></tr>
<tr><td>Key Words (max. 5 words)</td><td colspan="3">Education, Respiration, Renal, Cardiovascular, Pharmacology</td></tr>
<tr><td>Expected duration of the project (yrs)</td><td colspan="3">5 Years</td></tr>
<tr><td>Purpose of the project (as in Article 5)</td><td colspan="3"><table>
<tr><td>Basic research</td><td></td><td>No</td></tr>
<tr><td>Translational and applied research</td><td></td><td>No</td></tr>
<tr><td>Regulatory use and routine production</td><td></td><td>No</td></tr>
<tr><td>Protection of the natural environment in the interests of the health or welfare of humans or animals</td><td></td><td>No</td></tr>
<tr><td>Preservation of species</td><td></td><td>No</td></tr>
<tr><td>Higher education or training</td><td>Yes</td><td></td></tr>
<tr><td>Forensic enquiries</td><td></td><td>No</td></tr>
<tr><td>Maintenance of colonies of genetically altered animals</td><td></td><td>No</td></tr>
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<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td colspan="3">Our principal objective is to provide an education to postgraduate students in general pharmacology illustrating the consequences of administering agents in a whole body system. More specific goals are to:

1. Enable our students to undertake well controlled in vivo experiments with the long-term goal of increasing the number of UK scientists who have a high respect for, and awareness of the ethics of in vivo research, the 3Rs and legislative requirements.
2. Inculcate an understanding of formulating and testing hypotheses in in vivo experimental systems with the long-term goal of sustaining an integrative approach to biomedical research.
3. Monitor the achievement of our learning outcomes.

Realisation of these objectives will provide the licencees with a strong foundation upon which to undertake their own independent investigations, with due regard to animal welfare. In vivo experimentation is demanding in that it involves a level of complexity that is not encountered in computer simulations and in experiments on cells</td></tr>
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	and tissues. In addition to the need for surgical skills and the ability to maintain the well being of the animal under experimentation, the experimenter will become aware of the variables (species, strain, and environmental factors) that come into play when designing experiments on whole animals. It is only through practical 'hands-on' experience that useful knowledge can be gained about the requirements of successful *in vivo* experimentation. Such an appreciation of practical aspects *in vivo* experimentation is necessary because so much of what is undertaken in the biomedical science has, as its eventual goal, an application to the human condition. Hence, whole animal studies provide the bridge between phenomena identified in isolated cells and trials in human subjects. At present there is no alternative to using whole animal preparations for these studies. It should be noted that any surgical interventions carried out under this licence are non-recovery: i.e. the only pain that an animal will experience is the induction of anaesthesia by the injection of substances.
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 principal benefit of this programme will be the generation of scientists with a much better understanding of pharmacology than is possible with ex vivo work alone. A by product will be provision of scientists with the ability and confidence to undertake well-designed experiments in industry or in academia on whole animals when the requirement for such experiments is judged to be unavoidable.
What species and approximate numbers of animals do you expect to use over what period of time?	Principally rats and guinea-pigs, but a small number of rabbits, and ferrets will be used. Over the 5-year period: up to 260 animals may be used. This is based on our on-going experience of these experiments.
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?	It should be noted that ~90% of the experiments performed are non-recovery. The remaining animals will normally receive a single injection of a non-toxic substance and be killed 3 weeks later.
Application of the 3Rs	

1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	All the in vivo experiments are complemented by ex vivo or in vitro experiments. Where possible we have sought to reduce the number of animals required and use organ baths.
2. Reduction Explain how you will assure the use of minimum numbers of animals	The training and experience derived from this MSc taught course will enable students to integrate post-genomic molecular biology with *in vivo* function and, importantly, to design investigations reflecting careful ethical consideration. Such experience will both enhance their education and provide students with the integrative skills that are currently being re-emphasised as requirements in the pharmaceutical workplace. We will generally use and the minimum severity for each animal model that will give sensible results will be used. Wherever possible animals available from other users will be used as opposed to ordering animals specifically for the purpose of this work. It should be noted that tissue from the animals will be made available to other users at the end of the practical to reduce overall animal usage in for the university.
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.	Where surgical procedures are used, they are non-recovery procedures and the animals will only feel some transient discomfort associated with the induction of terminal general anaesthesia. If not non-recovery, then the animals will only experience the transient discomfort associated with the injection of a non-toxic substances to precondition a tissue response in ex vivo experiments. In this case the animals will be killed by a schedule 1 method and the tissue, surplus to requirements, will be shared among researchers.

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<tr><td>Project 2</td><td colspan="3">Education in pharmacology</td></tr>
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<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td colspan="3">The primary objectives of the project are:

1. Demonstration of the actions of catecholamines, their receptors, and cardiac drugs upon the heart and blood pressure.

2. Demonstration of the effects of diuretic drugs upon urine composition, renal output, the heart and blood pressure.

3. Demonstration of the actions of acetylcholine and its receptors upon the heart, blood pressure and other physiological parameters.

4. Demonstration of the effects of anaphylaxis and allergic responses in response to antigen exposure, and how these effects may be prevented by anti-histamine and other chemical</td></tr>
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	mediators. 5. Demonstration of the effects of natural mediators and drugs upon bronchial smooth muscle contraction and airways function as a model for human respiratory disease. 6. To monitor the success of the course, specifically how well the above objectives are met and more generally the value of this education to successful students in their future employment.
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 education and training of medical and biomedical science students are firmly based in the fundamental sciences. The ability to observe, collect, analyse and interpret experimental data is essential to the successful completion of their education. The power of using whole animals in experiments is illustrated by the integrated physiological response elicited by discreet events such as drug administration. For example, a drug administered for one purpose can often have other important effects in non-target tissues, which are not possible to observe in non-sentient species. Experiments using animals also allow students to develop an understanding of the strengths and weaknesses of biological experimentation. This allows students to appreciate the limitations of pharmacological research and development, and the validity of drug discovery. Students also observe first hand the variability inherent in biological measurements obtained from live animals in experimental settings. Students develop an acute awareness of the ethical issues of experiments on animals and the tenet of the 3 R's. Prior to practicals students attend a lecture covering ethics, animal welfare, and experimental design. In practical classes students engage in advanced discussions of the ethics of using animals for teaching and research purposes, and are

	invited to express their views on alternative teaching approaches such as computer simulations and videos. These discussions encourage a mature appreciation of animal experimentation, including the need to avoid unnecessary use of animals due to ill-considered, poorly designed or conducted experiments. Through participating in practicals involving living animals, students will develop unique understandings and experiences which are key for future careers in medicine and biomedical research. The pharmaceutical industry, one of the UK's major industries, is unable to recruit sufficient individuals with in vivo experience. Pharmaceutical companies universally support the development of individuals who appreciate and have skills in in vivo experimentation, and provide funding support via UK and EC research councils as well as the British Pharmacological and Physiological Societies.
What species and approximate numbers of animals do you expect to use over what period of time?	Principally rats and guinea-pigs, but a small number of rabbits and ferrets will be used. Over the 5-year period up to 720 animals may be used, which equates to less than one animal for every student taught in this period.
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 vast majority of the practicals are performed using deeply anaesthetised animals that do not recover from anaesthesia. Suffering is limited to transient discomfort associated with the induction of terminal general anaesthesia, perhaps similar to that experienced by patients undergoing a surgical procedure. In a small number of other practicals, animals receive one or two injections of a non-toxic substance and are then killed a few weeks later for post-mortem tissue analysis.
Application of the 3Rs	
1. Replacement	The practical classes form a small but

State why you need to use animals and why you cannot use non-animal alternatives	important part of a fully integrated course which uses a range of teaching methods including experiments using tissues in vitro or the students themselves, but also video recordings and simulations, lectures, seminars and tutorials. Whilst simulations or videos are adequate to illustrate basic principles, a full understanding of the nature of biomedical research and its attendant sources of error and variability, requires first hand exposure to experiments including use of living animals. Comparisons of physiology teaching and learning outcomes using computer simulations versus live animal demonstrations consistently emphasise the differences between these approaches, and their relative strengths. Students cannot gain a full appreciation of the nature of any branch of science from textbooks and lectures alone, and science education at all levels is supported by experimental demonstration of fundamental principles. In the case of pharmacology practicals, students apply the pharmacological and physiological concepts they learn in lectures and seminars to appreciate the complex, inter-related systems responsible, for example in the control of blood pressure. Moreover with a live animal, neither demonstrator nor student knows precisely what will happen next. This uncertainty teaches a respect for experimental observation and illustrates that scientific knowledge is not preordained but comes from measurement, analysis and hypothesis testing.
2. Reduction Explain how you will assure the use of minimum numbers of animals	We are conscious of the need to use the minimum number of animals in our practicals. A main means to achieve this is for students to work in groups. The size of each group is determined from teaching experience, student feedback, and also the nature of the practical. The number of animals used represents the best compromise between the minimum animal use and the greatest benefit to the students. In

	some cases students to observe an experienced individual demonstrate complex pharmacological and physiological principles in a challenging experimental model, and at the same time have the opportunity to discuss data with the demonstrator, as it emerges. In other cases group sizes are smaller so that students get the opportunity for hands-on experience and the independence of running the experiment and thinking more for themselves. It is common practice to use unwanted tissue from one practical in another practical, and also for unwanted tissue to be used by researchers. An ethical review process monitors the practicals with the aim to offer advice on minimising the number of animals used, identifying refinements to procedures, and maximising the benefits. Feedback is also relayed from various teaching committees, scientists, clinicians, vets, and the students themselves.
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 species have been selected as they best model major human health problems including cardiovascular and respiratory disease, and allergy, which are not easily modelled in vitro or non-sentient species. Rats, guinea pigs and ferrets are used to demonstrate cardiovascular and respiratory effects of drugs because they are able to tolerate large physiological changes. This allows testing of multiple manipulations thereby markedly increasing the value of the experiment. Guinea pigs are used to model allergy mechanisms because they generate a highly efficient antibody response. This represents a reduction and refinement because mice or rats would require multiple exposures over a considerable period, and even then it would not be guaranteed. The rabbit is used to demonstrate the actions of diuretics because smaller species do not produce urine at a

	sufficient rate to allow precise measurement of excreted ions. All surgical procedures are performed under non-recovery general anaesthesia, and animals will not experience pain beyond the transient discomfort associated with the induction of terminal anaesthesia. Surgical procedures, and anaesthesia induction and maintenance, are carried out by skilled demonstrators who stay with the animal for the duration of the experiment. Students are not involved in setting up the experiments.