Animals (Scientific Procedures) Act 1986

Non-technical summaries for projects granted during 2014

Volume 27

Projects with a primary purpose of: Maintenance of colonies of established genetically altered animals, not used in other procedures

Title and keywords

1. **Breeding and Maintenance of Genetically Altered Rodents**
    - Service Licence, Breeding and Maintenance

2. **Maintenance and breeding of Genetically Altered animals**
    - Breeding Genetically Altered animals

<table>
<tr><td>Project 1</td><td colspan="3">Breeding and Maintenance of Genetically Altered Rodents</td></tr>
<tr><td>Key Words (max. 5 words)</td><td colspan="3">Service Licence, Breeding and Maintenance</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></td><td>No</td></tr>
<tr><td>Forensic enquiries</td><td></td><td>No</td></tr>
<tr><td>Maintenance of colonies of genetically altered animals</td><td>Yes</td><td></td></tr>
</table></td></tr>
<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td colspan="3">This is a service licence that will enable the establishment, production and maintenance of various transgenic lines of rodents while a new or amended project licence is awaiting authorisation by the Home Office.</td></tr>
<tr><td>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)?</td><td colspan="3">Facilitates the temporary holding and maintenance of transgenic rodents awaiting transfer to a new or amended project licence of use thereby avoiding unnecessary wastage and import.</td></tr>
<tr><td>What species and approximate numbers of animals do you expect to use over what period of time?</td><td colspan="3">7000 Mice and 1000 Rats over 5 years</td></tr>
<tr><td>In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected</td><td colspan="3">Adverse effects will be dependent on the phenotype of the genetic strains.

Level of severity expected is mild to moderate</td></tr>
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level of severity? What will happen to the animals at the end?	dependent on the phenotype expression. This is a service licence and animals on this licence will be transferred to project licences where breeding and maintenance can continue and the animals may be moved into protocols of experimental use. Animals will be terminated by humane methods listed in Schedule 1 of ASPA.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	Although increasingly sophisticated in vitro methods are being developed, none either individually or in combination are capable of adequately replacing the complexity of the in vivo model afforded by a living animal.
2. Reduction Explain how you will assure the use of minimum numbers of animals	Increasingly investigators require the use of mice with complex genotypes. Design of breeding programmes and the use of Mendelian genetics will minimise the number of animals used in the start up colonies on this licence.
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 mouse is by far the most versatile vertebrate species for research using genetic techniques. Very extensive resources are available to support such work including complete genome sequences of several inbred strains. Before animals are imported from overseas we will consult mouse resources to ensure the strain is not already available within the UK. Where possible breeding schemes will be established to minimise the necessity for genotyping e.g. homozygous pairings. In most cases where genotyping is required the least invasive method will be selected e.g. ear biopsy ensuring that there is no additional suffering of the animals over and above normal good husbandry practices.

<table>
<tr><td>Project 2</td><td colspan="2">Maintenance and breeding of Genetically Altered animals</td></tr>
<tr><td>Key Words (max. 5 words)</td><td colspan="2">Breeding Genetically Altered animals</td></tr>
<tr><td>Expected duration of the project (yrs)</td><td colspan="2">5 years</td></tr>
<tr><td rowspan="8">Purpose of the project as in ASPA section 5C(3)</td><td></td><td>Basic research</td></tr>
<tr><td></td><td>Translational and applied research</td></tr>
<tr><td></td><td>Regulatory use and routine production</td></tr>
<tr><td></td><td>Protection of the natural environment in the interests of the health or welfare of humans or animals</td></tr>
<tr><td></td><td>Preservation of species</td></tr>
<tr><td></td><td>Higher education or training</td></tr>
<tr><td></td><td>Forensic enquiries</td></tr>
<tr><td>X</td><td>Maintenance of colonies of genetically altered animals</td></tr>
<tr><td>Describe the objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed)</td><td colspan="2">The aim of this project licence is to centralise the breeding of Genetically Altered (GA) animals for research teams who have the authority to use such models as part of their projects to ensure healthy colony maintenance with minimum wastage. The BSU has considerable expertise with the breeding of conditional and inducible gene systems which can sometimes have impaired fertility or fecundity, in collaboration with the researchers breeding strategies can be organised in order to maintain the line and also meet the project requirements underpinning the colony.</td></tr>
<tr><td>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)?</td><td colspan="2">This project deliveries a number of benefits including:
Effective liaison with end-user projects, to ensure the appropriate strains of the desired specification are bred (best model for the disease areas), with minimal wastage.
High level of technical expertise in the required breeding methodologies.
Transport of embryos or sperm, whenever possible, as opposed to animals.
On-site rederivation will render imported strains infection free for introduction into barrier accommodation and maintenance at a high health</td></tr>
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	status in optimum environmental conditions for the benefit of the animals wellbeing.
What species and approximate numbers of animals do you expect to use over what period of time?	Mice and rats, estimated numbers used are approximately 30 mice and 16 rats per line per month over the 5 year duration of the project.
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?	Animals will be supplied to projects authorised for their use otherwise they will be bred, humanely culled via a schedule one method or transferred to other institutions with the appropriate authority in place.
Application of the 3Rs	
1. Replacement State why you need to use animals and why you cannot use non-animal alternatives	*In vitro* work is an important preliminary step for assessing the biological function of a gene or protein and expression studies can be performed using cell lines, however, the interaction of transcription factors and other genes and the dynamic regulation that goes on via multiple systems will be absent *in vitro*. Therefore, research involving interesting target /molecule interactions must then proceed from these initial *in vitro* experiments to test the effects *in vivo* in a fully functioning biological system. In order to investigate the interaction between all the individual cells, growth factors, molecules etc involved, this work must be performed in animal models. It is hoped that results of the *in vivo* studies may also be used to refine and develop the *in vitro* models that will be useful in further experiments.
2. Reduction Explain how you will assure the use of minimum numbers of animals	A register will be kept of all existing strains held under this licence and new strains or crossing of existing strains to produce new combinations added to the register. This will detail the nature of the mutation, any adverse phenotypes, husbandry requirements and breeding efficiency. Breeding will be optimised, wherever possible, to produce only the genotype required e.g. Homozygous breeding pairs to produce homozygous offspring if that is the only genotype required by a research project, thus reducing the need to

	breed surplus animals. The considerable experience and expertise available in animal husbandry and breeding of genetically altered lines within the BSU will ensure that breeding programmes are co-ordinated to ensure optimal fecundity and minimal surplus. Breeding performance will be monitored and intervention levels pre-determined depending on the line/method of breeding. A good understanding of laboratory animal science will ensure careful management of colonies, matching supply to demand and thus reducing the production of surplus animals.
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.	This licence will be used to breed and supply genetically altered rodents. As this is a service licence the species of animals bred under its' authority is determined by the projects it supplies to. Mice are the recognised species for work involving genetically altered animals. There are standard protocols that (utilised in this Project Licence) and acknowledged benefits from their use. Rats are used more rarely than mice but are needed for some specific projects e.g. Nude rats (rnu/rnu) are used in cancer projects as their immunocompromised status allows them to grow subcutaneously implanted tumours. Embryos, gametes, sperm and ovarian tissue will be collected from donor strains. They may be cryopreserved or used for the following purposes. • Fresh or frozen embryos/sperm will be used to rederive an infected strain to improve its health status • Gametes, embryos/sperm or/and tissue will be cryopreserved to store a line in support of the breeding colonies • Gametes, embryos/sperm or/and tissue will be used to replace a strain for storage where there is no longer a demand avoiding 'wastage' from 'tick over' breeding • Gametes, embryos/sperm or/and tissue will be used where possible instead of live animals to transfer strains to other locations, especially off site and abroad