Standard GA B&M Protocols

Protocol 1

Title

|  |
| --- |
| Superovulation |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| Superovulation to generate ova or blastocysts |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Mild |
| *Select from the drop-down list.* |

What proportion of animals will experience this severity?

|  |
| --- |
| All animals |

Why are you proposing this severity category?

|  |
| --- |
|  |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| * OBJECTIVE A |
| * OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Oocytes or embryos harvested post mortem. |

Animals used in this protocol

## Which types of animals would you like to add to this protocol?

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| * Adult |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| Yes |

How did these animals start their use?

Describe the procedures that have been applied to animals that will continue their use on to this protocol.

|  |
| --- |
| Genetically altered animals (with or without associated wild types) for use in this protocol may be obtained from Protocol 5 ‘Breeding and maintenance of genetically altered animals’ (mild) [or Protocol 6 ‘Breeding and maintenance of genetically altered animals’ (moderate)] [delete as appropriate]; or other project licences with authority to breed and maintain genetically altered animals of a type authorised in this project, and to provide them for use on other projects. |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| Yes |

Describe any procedure that may have been applied to these animals, and why you are choosing to re-use them.

|  |
| --- |
| Animals that have been kept alive and maintained under the supervision of the NVS may be re-used in this protocol when advised by the NVS. |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g.100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

|  |
| --- |
| Yes |

Which general types or strains will you be using and why?

|  |
| --- |
| GA mouse lines *e.g.* XXX for XXX. |

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

|  |
| --- |
| No |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia.

When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Administration of agents to induce superovulation *e.g.* gonadotrophin, hormones or other agents administered by intra-peritoneal or subcutaneous injections typically twice but rarely up to four times (AA). |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Transient discomfort and no lasting harm. |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| N/A |
| The additional condition for the administration of substances and withdrawal of fluids will be applied by the Inspector. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| Any animal showing any deviation from normal health or wellbeing will be immediately killed by a Schedule 1 method. |

## Step 2 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| If embryos are needed these animals will also be mated. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| N/A |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| Genetically altered animals used in this protocol are not expected to exhibit any harmful phenotype but, if they do, they will be immediately killed by a Schedule 1 method.  Where the immune status of the animals might compromise health, they will be held in a barrier environment.  Females will be of an appropriate size, if they are to be mated.  Over vigorous males will be replaced. |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| No |

Protocol justification

a) the most appropriate scientific approach? ​

|  |
| --- |
| N/A |

b) the most refined for the purpose?

|  |
| --- |
| N/A |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| N/A |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| N/A |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| N/A |

Will you be administering substances for experimental purposes?

|  |
| --- |
| Yes |

How will you assess the suitability of these substances, and minimise the unnecessary harms arising from their administration given the particular strain or type of animal you will be using?

When assessing suitability, state how you will consider toxicity, efficacy, and sterility.

|  |
| --- |
| Substances used are commercially available and not known to have toxic side effects. |

How will you determine an appropriate dosing regimen? ​

Include routes, dosage volumes, frequencies, and durations.

|  |
| --- |
| Routes, dosage volumes, frequencies and durations will be obtained from published literature. |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Killed |

*Ensure that the methods of killing to be used are described in the final step of this protocol.*

Method of killing

|  |
| --- |
| * Schedule 1 method​ |

Protocol 2

Title

|  |
| --- |
| Generation of Founders |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| The creation or re-derivation of genetically altered embryos. |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Mild |
| *Select from the drop-down list.* |

What proportion of animals will experience this severity?

|  |
| --- |
| All animals. |

Why are you proposing this severity category?

|  |
| --- |
| Founder stock animals are not expected to exhibit a harmful phenotype prior to weaning. |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| OBJECTIVE A |
| OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Genetically altered embryos. |

Animals used in this protocol

## Which types of animals would you like to add to this protocol?

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| * Embryo and egg |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| No |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| No |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g. 100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

|  |
| --- |
| Yes |

Which general types or strains will you be using and why?

|  |
| --- |
| GA mouse lines XXX for XXX. |

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

|  |
| --- |
| No |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Generation of genetically altered embryos by in vitro manipulation and/or fertilisation. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

## Step 2 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Genetically altered embryos will be implanted into pseudopregnant females being used under Protocol 3 and allowed to develop. The resulting offspring, the “founder stock” will be maintained and bred under Protocol 5 [or Protocol 6]. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| N/A |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| Any animal will be immediately killed by Schedule 1 method if it shows evidence of suffering that is greater than minor and transient or in any way compromises its normal behaviour. |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| No |

Protocol justification

a) the most appropriate scientific approach? ​

**The methods used are well established in the published literature and in our laboratories.**

|  |
| --- |
| N/A |

b) the most refined for the purpose?

|  |
| --- |
| N/A |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| N/A |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| N/A |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| N/A |

Will you be administering substances for experimental purposes?

|  |
| --- |
| No |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Killed |

*Ensure that the methods of killing to be used are described in the final step of this protocol.*

Method of killing

|  |
| --- |
| * Schedule 1 method​ |
| * Continued use on another protocol in this project |

Please state the relevant protocol.

|  |
| --- |
| Founder stock will be maintained and bred on protocol 5 ‘Breeding and maintenance’ (mild) [or Protocol 6 'Breeding and maintenance' (moderate)]. |

Protocol 3

Title

|  |
| --- |
| Embryo recipients |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| Transfer embryos into recipients of appropriate health status. |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Moderate |
| *Select from the drop-down list.* |

What proportion of animals will experience this severity?

|  |
| --- |
| …% of animals will experience moderate severity. |

Why are you proposing this severity category?

|  |
| --- |
| Animals undergoing surgical embryo transfer will experience transient post-operative pain and discomfort.  Animals undergoing non-surgical embryo transfer will experience mild transient discomfort and no lasting harm. |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| OBJECTIVE A |
| OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Genetically altered mice |

Animals used in this protocol

## Which types of animals would you like to add to this protocol?

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| * Embryo and egg |
| * Adult |
| * Pregnant adult |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| No |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| Yes |

Describe any procedure that may have been applied to these animals, and why you are choosing to re-use them.

|  |
| --- |
| Animals that have been kept alive and maintained under the supervision of the NVS may be re-used in this protocol, when advised by the NVS. |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g. 100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

|  |
| --- |
| Yes |

Which general types or strains will you be using and why?

|  |
| --- |
| Genetically altered mice XXX for XXX. |

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

|  |
| --- |
| No |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Female mice will be rendered pseudo-pregnant by mating with a sterile male. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

## Step 2 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Embryos will be implanted surgically (AB) or non-surgically (AA/AB) into the reproductive tract of the pseudo-pregnant mice. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Infection  Wound dehiscence  Surgical or anaesthetic complications  Poor recovery from surgery/anaesthesia  Pain  Distress  Transient discomfort |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| N/A |
| The additional condition for the administration of substances and withdrawal of fluids will be applied by the Inspector. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| N/A |
| The additional condition for the administration of substances and withdrawal of fluids will be applied by the Inspector. |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| N/A |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| N/A |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| No |

Protocol justification

a) the most appropriate scientific approach? ​

|  |
| --- |
| N/A |

b) the most refined for the purpose?

|  |
| --- |
| Non-surgical embryo transfer methods will be used where the success rate matches that of surgical embryo transfer methods. |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| N/A. |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| N/A |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| N/A |

Will you be administering substances for experimental purposes?

|  |
| --- |
| No |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Killed |

*Ensure that the methods of killing to be used are described in the final step of this protocol.*

Method of killing

|  |
| --- |
| * Schedule 1 method​ |

Protocol 4

Title

|  |
| --- |
| Vasectomy |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| To produce sterile male mice for mating to obtain pseudo-pregnant female mice to be used for embryo transfer. |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Moderate |

What proportion of animals will experience this severity?

|  |
| --- |
| All animals |

Why are you proposing this severity category?

|  |
| --- |
| All animals will undergo surgery for vasectomy and will experience transient post-operative pain and discomfort. |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| OBJECTIVE A |
| OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Sterile male mice. |

Animals used in this protocol

## Which types of animals would you like to add to this protocol?

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| Adult |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| No |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| Yes |

Describe any procedure that may have been applied to these animals, and why you are choosing to re-use them.

|  |
| --- |
| Animals that have been kept alive and maintained under the supervision of the NVS may be re-used in this protocol, when advised by the NVS. |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g.100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

|  |
| --- |
| No |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| The vas deferens will be exposed and sectioned bilaterally by a scrotal approach (AB). |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Infection  Wound dehiscence  Pain  Distress  Surgical or anaesthetic complications  Poor recovery from anaesthesia/surgery |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| N/A |
| The additional condition for the administration of substances and withdrawal of fluids will be applied by the Inspector. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| N/A |
| The additional condition for the administration of substances and withdrawal of fluids will be applied by the Inspector. |

## Step 2 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| After a post-op recovery period (minimum 2 weeks) sterility will be assessed, e.g. by mating the vasectomised male with normal females. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

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Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| N/A |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| N/A |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| No |

Protocol justification

a) the most appropriate scientific approach? ​

|  |
| --- |
| N/A |

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

b) the most refined for the purpose?

|  |
| --- |
| Where possible genetically altered sterile males will be used instead of vasectomised males.  The scrotal approach is more refined than the abdominal approach. |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| N/A |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| N/A |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| N/A |

Will you be administering substances for experimental purposes?

|  |
| --- |
| No |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Kept alive |

Protocol 5

Title

|  |
| --- |
| Breeding and maintenance of genetically altered mice (mild) |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| To produce, maintain and provide genetically altered mice. |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Mild |
| *Select from the drop-down list.* |

What proportion of animals will experience this severity?

|  |
| --- |
| All animals  OR  Few – we expect the phenotype to be sub-threshold |

Why are you proposing this severity category?

|  |
| --- |
| Animals are not expected to show harmful phenotypes that are more than minor or transient. |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| * OBJECTIVE A |
| * OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Genetically altered mice |

Animals used in this protocol

## Which types of animals would you like to add to this protocol?

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| * Embryo and egg |
| * Neonate |
| * Juvenile |
| * Adult |
| * Pregnant adult |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| Yes |

How did these animals start their use?

Describe the procedures that have been applied to animals that will continue their use on to this protocol.

|  |
| --- |
| Founder stock created under Protocol X will be maintained and bred under this protocol.  AND/OR  Genetically altered animals (and associated wild type controls) for use in this protocol may be obtained from other projects with authority to breed and maintain genetically altered animals of a type authorised in this project, and to provide them for use on other projects. |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| No |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g. 100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals? \_

|  |
| --- |
| Yes |

Which general types or strains will you be using and why?

|  |
| --- |
| Genetically altered mice XXX for XXX. |

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

|  |
| --- |
| No |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Breeding of genetically altered mice by conventional breeding methods |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

## Step 2 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Tissue biopsy to determine genetic status by one of the following methods:   * ear biopsy (AA/AB) * blood sampling (AA/AB) * hair sampling (AA/AB) * Removal of tip of tail (AB) if scientifically necessary.   Rarely, due to technical problems during analysis, a second sample may be taken using the least invasive method. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Minor and transient pain and discomfort. |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| For the tail tip no more than 0.3 cm will be removed.  Pain will be controlled by using analgesics. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| Any animal will be immediately killed by Schedule 1 method if it shows signs of suffering that is greater than minor and transient or in any way compromises normal behaviour. |

## Step 3 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Maintenance of animals by methods appropriate to their genetic alteration until they reach a maximum of 15 months of age. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Some animals may have an altered immune system making them more susceptible to infection. |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| Animals with altered immune status will be maintained in a barrier environment thereby minimising the likelihood of compromising health. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| Any animal will be immediately killed by Schedule 1 method if it shows signs of suffering that is greater than minor and transient or in any way compromises normal behaviour unless moved on to another protocol for a specific purpose (continued use).  Animals exhibiting any unexpected harmful phenotypes will be killed (Schedule 1), or in the case of individual animals of particular scientific interest, advice will be sought promptly from the local Home Office Inspector. |

## Step 4 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Terminal procedures:   * Exsanguination and completed by a Schedule 1 method (AC); * perfusion fixation (AC). |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| Animals produced under this protocol are not expected to exhibit any harmful phenotype. |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| Any animal will be immediately killed by Schedule 1 method if it shows signs of suffering that is greater than minor and transient or in any way compromises normal behaviour. Animals exhibiting any unexpected harmful phenotypes will be killed (Schedule 1), or in the case of individual animals of particular scientific interest, advice will be sought promptly from the local Home Office Inspector. |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| No |

Protocol justification

Why is each type of animal, experimental model, and/or method selected for this protocol:

a) the most appropriate scientific approach?

|  |
| --- |
| N/A |

b) the most refined for the purpose?

|  |
| --- |
| Tail biopsy will only be taken if more refined genotyping methods are not suitable scientifically. |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| N/A |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| N/A |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| N/A |

Will you be administering substances for experimental purposes?

|  |
| --- |
| No |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Killed |

*Ensure that the methods of killing to be used are described in the final step of this protocol.*

Method of killing

|  |
| --- |
| * Schedule 1 method​ |

|  |
| --- |
| * Kept alive (genetically normal mice) |
| * Continued use on another protocol in this project |

Please state the relevant protocol.

|  |
| --- |
| <<<INSERT animal type(s) HERE>>> may continue to be used on <<<INSERT protocol number(s) HERE>>> of this project. |
| *The Inspector will need to draft a bespoke Authorisation to authorise continued use onto other protocols.* |

|  |
| --- |
| * Continued use on other projects |
| *The Inspector will need to draft a bespoke Authorisation to authorise continued use onto other projects.* |

Protocol 6

Title

|  |
| --- |
| Breeding and maintenance of genetically altered mice (moderate) |

Protocol details

Briefly describe the purposes of this protocol

Ensure that you state any relevant regulatory guidelines.

|  |
| --- |
| To produce, maintain and provide genetically altered mice. |

Given the controls and limitations in place, what is the highest severity that an animal could experience in this protocol?

|  |
| --- |
| Moderate |
| *Select from the drop-down list.* |

What proportion of animals will experience this severity?

|  |
| --- |
| Approximately X% of animals are likely to experience moderate levels of severity. This is because {...}. |

Why are you proposing this severity category?

|  |
| --- |
| We will be using strain X of genetically altered mice and this strain will show progressive ...{...}. from {...} weeks of age until reaching {....} at 12 weeks of age.  *Repeat this for all the strains that are likely to develop a phenotype.* |

Select the establishments or POLEs where this protocol will be carried out.

Select all that apply.

|  |
| --- |
| * Place A |
| *Select from the drop-down list.* |

Which of your objectives will this protocol address?

Select all that apply.

|  |
| --- |
| * OBJECTIVE A |
| * OBJECTIVE B |
| *Select from the drop-down list.* |

What outputs are expected to arise from this protocol?

For example, test results, phenotypic information, or products.

|  |
| --- |
| Genetically altered mice. |

Animals used in this protocol

|  |
| --- |
| Mice |
| *Select from the drop-down list.* |

Which life stages will be used during this protocol?

Select all that apply

|  |
| --- |
| * Embryo and egg |
| * Neonate |
| * Juvenile |
| * Adult |
| * Pregnant adult |
| *Select from the drop-down list.* |

Will any animals coming on to this protocol be classed as ‘continued use’?

‘Continued use’ describes animals that are specifically genetically altered and bred for scientific use or animals that have had procedures applied to them in order to be prepared for use in this protocol.

|  |
| --- |
| Yes |

How did these animals start their use?

Describe the procedures that have been applied to animals that will continue their use on to this protocol.

|  |
| --- |
| Genetically altered animals (and associated wild type controls) for use in this protocol may be obtained from other projects with authority to breed and maintain genetically altered animals of a type authorised in this project, and to provide them for use on other projects. |

Will you be re-using animals on to this protocol?

‘Re-use’ describes using animals again for a new experiment when you could equally use a naïve animal to get the same results.

|  |
| --- |
| No |

What is the maximum number of animals that will be used on this protocol?

|  |
| --- |
| e.g. 100 |

What is the maximum number of uses of this protocol per animal?

For example, if some animals will go through this protocol three more times after their first use, the number of uses will be four.

|  |
| --- |
| 1 |

Genetically altered animals (GAA)

Will this protocol use any genetically altered animals?

|  |
| --- |
| Yes |

Which general types or strains will you be using and why?

|  |
| --- |
| We will be using genetically altered mice strain X that overexpresses/does not expresses gene X. |

Do you expect any of these GAAs to show a harmful phenotype with welfare consequences?

|  |
| --- |
| Yes |

Why are each of these harmful phenotypes necessary?

|  |
| --- |
| To determine whether gene X plays a role in the development of disease X, we will create mice that either don’t express the gene or overexpress the gene which leads to the clinical findings {...}. |

How will you minimise the harms associated with these phenotypes?

Ensure that you include any humane endpoints that you will use.

|  |
| --- |
| Some lines may be embryonic lethal or lethal before adulthood (e.g. XXX), and such lines will be made as conditional knockouts or be maintained as heterozygotes. |

Steps

## Step 1 (mandatory)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Breeding of genetically altered mice by conventional breeding methods |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| No |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

## Step 2 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Tissue biopsy to determine genetic status by one of the following methods:   * ear biopsy (AA/AB) * blood sampling (AA/AB) * hair sampling (AA/AB) * Removal of tip of tail (AB) if scientifically necessary.   Rarely, due to technical problems during analysis, a second sample may be taken using the least invasive method. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| Minor and transient pain and discomfort. |

How will you monitor for, control, and limit any of these adverse effects?​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| For the tail tip no more than 0.3 cm will be removed.  Pain will be controlled by using analgesics. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| Any animal will be immediately killed by Schedule 1 method if it shows signs of suffering that is greater than minor and transient or in any way compromises normal behaviour. |

## Step 3 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Maintenance of animals by methods appropriate to their genetic alteration until they reach a maximum of 15 months of age. |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| Yes |

What are the likely adverse effects of this step? ​

State the signs of each adverse effect, including the likely incidence, and the anticipated degree and duration of suffering.

|  |
| --- |
| For example: Strain X will show the following clinical signs:  - overtly normal up to 4 weeks of age;  - progressive {.....} until reaching .{....} .. at 12 weeks of age. |

How will you monitor for, control, and limit any of these adverse effects? ​

If adverse effects can't be prevented, how will you attempt to ameliorate their initial signs?

|  |
| --- |
| For example: Some lines may be embryonic lethal or lethal before adulthood (*e.g.* X) and such lines will be made as conditional knockouts or be maintained as heterozygotes.  For each line, a detailed phenotypic assessment will be made, for inclusion in a mouse passport. |

What are the humane endpoints for this step?

This would be the point at which you would kill the animal to prevent further suffering.

|  |
| --- |
| For example: Breeding stock will be killed after the first litter is weaned, and before onset of {...}.  Offspring will be killed before 4 weeks of age or at the onset of clinical signs if earlier unless required for experimental use when they will be transferred for continued use. |

## Step 4 (optional)

Describe the procedures that will be carried out during this step.

Explain where one or more steps are repeated in one experiment, list any alternative techniques within a step (e.g. dosing routes), and include all procedures performed under terminal anaesthesia. When describing the technical aspects of a step, be broad enough to be flexible when the variation does not impact on animal welfare (e.g. use "antibiotic" instead of "penicillin"). Finally, avoid specifying volumes and frequencies when they do not impact on animal welfare.

|  |
| --- |
| Terminal procedures:   * exsanguination and completed by a Schedule 1 method (AC); * perfusion fixation (AC). |

Will this step involve the use of neuromuscular blocking agents (NMBAs)?

|  |
| --- |
| No |

Is this step optional?

|  |
| --- |
| Yes |

Do you expect this step to have any adverse effects for the animals?

|  |
| --- |
| No |

Animal experience

Summarise the typical experience or end-to-end scenario for an animal being used in this protocol.

Consider the cumulative effect of any combinations of procedures that you may carry out.

|  |
| --- |
| For example: Breeding stock will be only allowed one breeding cycle and offspring will be killed or transferred to an experimental protocol before the age of {x weeks}. During that time, they should show no more than XXX. |

Describe the general humane endpoints that you will apply during the protocol.

These will be in addition to the endpoints stated for each step.

|  |
| --- |
| Example: Any mouse that shows XXX will be immediately killed (Schedule 1) |

Experimental design

Will this protocol generate quantitative data?

|  |
| --- |
| *No* |

Protocol justification

Why is each type of animal, experimental model, and/or method selected for this protocol:

a) the most appropriate scientific approach? ​

|  |
| --- |
| N/A |

b) the most refined for the purpose?

|  |
| --- |
| Example: Tail biopsy will only be taken if more refined genotyping methods are not suitable scientifically. We need mice aged { } with genetic alterations XXX to achieve objective A. |

For each model and/or method, what is the scientific need for the expected clinical signs?

|  |
| --- |
| We need mice aged { } with genetic alterations XXX to achieve objective A. |

Why scientifically do the animals need to suffer to this degree?

|  |
| --- |
| We need animals that are showing {clinical signs} in order to { }… |

Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?

|  |
| --- |
| An earlier humane end point cannot be achieved because XXX. |

Will you be administering substances for experimental purposes?

|  |
| --- |
| No |

Fate of animals

What will happen to animals at the end of this protocol? ​

Select all that apply

|  |
| --- |
| * Killed |

*Ensure that the methods of killing to be used are described in the final step of this protocol.*

Method of killing

|  |
| --- |
| * Schedule 1 method​ |

|  |
| --- |
| * Kept alive (genetically normal mice) |
| * Continued use on another protocol in this project |

Please state the relevant protocol.

|  |
| --- |
| <<<INSERT animal type(s) HERE>>> may continue to be used on <<<INSERT protocol number(s) HERE>>> of this project. |
| *The Inspector will need to draft a bespoke Authorisation to authorise continued use onto other protocols.* |

|  |
| --- |
| * Continued use on other projects |
| *The Inspector will need to draft a bespoke Authorisation to authorise continued use onto other projects.* |