NON-TECHNICAL SUMMARY

Induction, assessment and prevention of adhesions

Project duration

1 years 0 months

Project purpose

- (b) Translational or applied research with one of the following aims:
  - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants.
  - (ii) Assessment, detection, regulation or modification of physiological conditions in man, animals or plants.

Key words

No answer provided

Retrospective assessment

The Secretary of State has determined that a retrospective assessment of this licence is not required.

Objectives and benefits

Description of the project's objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.

What is the aim of this project?
Post-surgical adhesions (PSAs) consist of fibrous tissue which sometimes grows excessively and can lead to constriction of the bowel and other internal structures, cause significant pain and even result in female sterility.

This licence will predominantly cover work done as part of our device development strategy and as such will focus on novel minimally invasive devices and new/modified techniques related to them. However, the intention is also to use this as a service licence to investigate other devices/compounds with the ability to aid in the reduction of the problems associated with adhesions.

In a systematic review of 87 studies including 110,076 patients the incidence of small-bowel obstruction due to PSAs was 9% which is equal to 9,906 patients over a period of five years. If these figures are extrapolated to include adhesions at other sites (which have not yet been exposed to systematic review) it is likely that an excess of 10,000 patients per year could benefit from an effective PSA prevention strategy.

**Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.**

**What are the potential benefits that will derive from this project?**

The long-term benefit is the reduction or prevention of post surgical adhesions in both humans and animals will reduce post-operative complications, enable efficient recovery to normal movement, reduce or remove the need to carry out subsequent surgery to remove adhesions and thus improve patient welfare, reduce hospital in-patient time and reduce the financial implications.

The short-term benefits will be the development of new devices through initial in-vivo testing and the generation of data for submission to regulatory authorities.

**Species and numbers of animals expected to be used**

**What types and approximate numbers of animals will you use over the course of this project?**

Over the 6 months of this licence we would aim to use approximately 20 sheep and 60 pigs.

**Predicted harms**

**Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.**

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 models we use create adhesions, but we do not let these adhesions become painful to the animals as we treat just after creation to assess reduction or prevention and we know from previous studies that the treatments we use have good potential to reduce or prevent PSAs so we would regard this licence as only moderate in its severity. Some animals will be recovered from surgery and will be monitored for up to 6 months after the initial surgery. This may include repeated anaesthetics for the purposes of biopsy and/or non-invasive imaging. Any animals who show excessive signs of distress will be put down and examined in an attempt to determine the cause and also to assess the effect of the treatment applied to them. At the end of each study the animals will be put down and the tissue taken and examined to assess the efficacy of the treatment, also, where possible, tissue will be taken for other studies and/or educational purposes in an effort to maximise the usage and reduce overall number of animals used.

Replacement

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

The formation of adhesions is a complex process involving many different components within the body (blood, lymph, enzymes, etc) all interacting and as such a complete live animal is needed to form adhesions for evaluation and subsequent treatment. Prior to live animal studies, procedures, materials or devices to be assessed will, where possible, be tested on cells or tissues in order to keep animal use to a minimum.

Reduction

Explain how you will assure the use of minimum numbers of animals.

All potential treatments, procedures or devices transitioning from the laboratory into live animal testing will go via pilot studies involving small numbers (typically 3) of animals - this is to be sure that the laboratory prediction is borne out in live tissues.

For many of the studies carried out under these protocols, several sites of injury can be induced in the same animal which allows us to reduce the number of animals required to produce scientifically relevant data. Also, the ability to use adjacent or remote tissues from the same animal as internal or autologous controls again allows a reduction in the number of animals required overall.

For those studies carried out under Good Laboratory Practice (GLP) compliance, a regulatory process required by the Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) for all pre-clinical studies leading to requests for use in man, statistically robust appropriate information must be derived and this typically requires between 6 and 10 animals per experimental group to satisfy these parameters.

The ability to remove organs and tissues under terminal anaesthesia from animals in one study to be used for in vitro or ex vivo studies or transplantation/implantation or to be used for training reduces the need to retrieve these organs or tissues from dedicated donors thus reducing the number of animals required overall.
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 models we use have been evolved over the last 20 years and are as refined as we can currently achieve. We use smaller species (mice and rats) for initial studies to confirm that the laboratory prediction is borne out in live tissues but often need to use more appropriately sized animals (i.e. a similar size to humans) for many studies. Using a range of assessments including non-invasive imaging (e.g. X-ray or Ultrasound) has further refined our techniques allowing us to obtain more information whilst minimising the impact on the animals' welfare.

For some direct application treatments, to establish representative sized defects and relevant treatment doses, large animals are required. Also, for the new procedures, instrumentation is designed for humans and a representatively sized animal will therefore have to be used. There are some areas of anatomy which are specifically recognised within different species as best models – e.g. for meniscal cartilage the sheep is deemed more anatomically similar to humans than is the pig, while for bowel and vasculature the pig is deemed more representative of the human than the sheep. Choices of species will be dependent on the anatomic site under investigation.

Appropriate monitoring of animals post-surgery and intervention if necessary with pain relief medication will ensure animal comfort. Our experience is that the animals are not in any pain during these studies probably because most are treated and those that are not are not allowed to progress to the level of adhesion formation where humans would present with symptoms.