Home Office

Who or what will benefit from these outputs, and how?

In the first instance the data generated from studies will aid the researchers in the selection and characterisation of new vaccines and antibody treatments which will lead to their further development (e.g. in clinical trials) and could potentially lead to new therapies for respiratory diseases being introduced to the market.

Long term, these products have the potential to significantly enhance the quality of life for people suffering these chronic diseases or potentially cure them. This will benefit the whole society via reduction in absenteeism from work or school and reduction in demand on health services.

How will you look to maximise the outputs of this work?

Our commercial client will, where not confidential, look to publish the information via scientific publications and conference presentations in addition to patent applications.

One of the key goals of our academic clients will be to publish the results via scientific publications conference presentations, in order to promote the general advancement of the fields studied.

Species and numbers of animals expected to be used

- Mice: 3600
- Rats: 3600
- Guinea pigs: 2100

Predicted harms

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

Explain why you are using these types of animals and your choice of life stages.

Typically, what will be done to an animal used in your project?

After arrival all animals will be allowed at least 7 days to become acclimatised to the unit.

After which the animals will be dosed with potential new vaccines or antibody treatments. These animals may receive up to total of 28 doses. A certain proportion of the animals will be used to investigate the effects and pharmacokinetic properties of the assigned treatment after single and multiple doses. Blood samples, and tissues taken post-mortem are analysed.

The next subset of animals will used to study the efficacy of the candidate vaccines or antibody treatment. The animals will be studied in a mechanistic model of respiratory inflammation, where they are challenged with the respiratory virus the treatment is targeted for, into the lung and the efficacy of the treatment on the inflammatory response investigated.

Another subset of animals will be studied in the ovalbumin or house dust mite induced respiratory disease models of either asthma or COPD. These animals will receive one of more doses of inflammatory agents and will develop a phenotype very similar to the human diseases. The ability of the candidate vaccines to alter this phenotype will be studied.

The last subset will also be studied in the same respiratory disease models, with an added viral challenge to study the ability of the candidate vaccines or antibody treatment to reduce viral exacerbations.

A proportion of the animals in each study will receive vehicle only these will be the control animals and are the group most likely to show the possible adverse effects. From experience we know the dose of challenge agent that gives the maximum response we are measuring while keeping any adverse effects low if at all. This is especially important for these control animals.

While the maximum length a study could run for under this licence is 9 months, this would be very rare and the justification to run such a study would need to be strong. The vast majority of studies will be much short with a typically study lasting 2 to 3 weeks from starting the study to the final sampling time point. This would typically be a week of pre-dosing followed by a challenge and up to 2 weeks of sampling post-challenge.

What are the expected impacts and/or adverse effects for the animals during your project?

Studies conducted under this licence may induce some adverse effects in some of the animals. Typical adverse effects include changes in appearance, for example, minor changes in respiratory patterns ruffled fur, or changes in behaviour, e.g. the animals may become subdued. Other effects may include reduction in body weight and/or reduced eating. The larger proportion of animals used in these studies will, however, not experience any noticeable adverse effects.

Expected severity categories and the proportion of animals in each category, per species.

What are the expected severities and the proportion of animals in each category (per animal type)?

For the majority of animals, the severity level will be mild. However, as stated above, in some studies the animals may experience some adverse effects, but these would only cause the animal a moderate level of distress which will in most cases be transient.

What will happen to animals at the end of this project?

- Killed

Replacement

State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.

Why do you need to use animals to achieve the aim of your project?

Understanding the mechanisms of action and assessing the effectiveness of potential new vaccines or antibody treatment in respiratory diseases requires the presence of a fully developed and functional respiratory system. Currently this cannot be reproduced outside of a living organism. Indeed, the assessment of the efficacy of candidates for respiratory diseases cannot be efficiently modelled in vitro due to the complexities of the lung microenvironment and the involvement of the immune system in these diseases. This cannot be fully replicated in a laboratory setting.

Which non-animal alternatives did you consider for use in this project?

Novel vaccines or antibody treatments selected for testing in the models contained within this licence will have to have been through a defined screening cascade of in vitro assays prior to testing in vivo

Reduction

Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.

How have you estimated the numbers of animals you will use?

A typical experiment may include up to 60 animaln, šiimaUš5M ei

Refinement

Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.

Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

Mice rats and guinea pigs are the ideal organisms for these investigations:

They are the long-standing choice for respiratory research. There is an immense spectrum of well-characterised models developed over the years which cause minimal distress and suffering while providing meaningful data This is due to the similarities between the respiratory and immune systems in these animals and human. The commonly used laboratory strains of animals are well phenotypically and genetically characterised. Guinea pigs are widely used for respiratory research because their airways are generally more sensitive than other rodents, especially to allergens.

Secondly, because of the large number of well-characterised models, there are reagents available permitting the thorough, incisive, and comprehensive analysis of samples collected allowing for the maximum amount of information to be obtained from the experiments undertaken.

To minimise discomfort of repeated procedures such as anaesthesia, we will combine treatments under a single anaesthetic event wherever possible. The anaesthesia will preferably entail the use of inhalation agents whenever possible. Least invasive route of substance administration and needle gauge will be used where possible.

Negative control groups (baseline groups) will be minimised whenever statistically feasible.

Why can’t you use animals that are less sentient?

The human respiratory and immune systems are intricately complex and modelling it for assessment of new medicines requires models in vertebrate animals whose systems have been studied and can be, to a good degree, compared to human. Mice, rats and guinea pigs are the lowest vertebrate group on which plethora of reliable information on the function of the systems are available and where well characterised and minimal severity respiratory models have been developed.

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?

To minimise discomfort of repeated procedures such as anaesthesia, we will combine treatments under a single anaesthetic event wherever possible. The anaesthesia will preferably entail the use of inhalation agents whenever possible. Least invasive route of substance administration and needle gauge will be used where possible. Negative control groups (baseline groups) will be minimised whenever statistically feasible.

All animals will receive appropriate operative care in terms of anaesthesia and pain management both during and after the procedure.

In house expertise further enhances animal welfare, by providing close collaboration with dedicated animal care staff and veterinary consultants, and ready access to highly skilled advice.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?

We will follow the NC3Rs guidelines on the "Responsibility in the use of animals in bioscience research" and consult all the relevant references listed therein. (Reference: NC3Rs/BBSRC/Defra/MRC/NERC/Royal Society/Wellcome Trust (2019 Responsibility in the use of animals in bioscience research: expectations of the major research councils and charitable funding bodies. London: NC3Rs.

Animals will continually be monitored for signs of pain and distress, especially post-challenge, by use of the grimace scale;
https://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/MGS%20Manual.pdf.