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

Objectives and benefits

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

What's the aim of this project?

To understand the interplay between calf and maternal factors during immune development. To

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)?

Calves: 100% mild

Cows: 100% mild

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

- Kept alive
- Rehomed

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?

Animal models are required for the study of immune development and response to disease in a commercial farming environment. It is not possible to replicate the complex interactions between the animal, the environment and disease pathogens within a test tube or using other laboratory techniques alone. Furthermore, by performing this study on animals within a commercial environment, the results of this project will be highly applicable to calf-rearers, which will maximise the impact of the study outcomes and their relevance.

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

A literature search using the search engines Pubmed and Agricola were used following established guidelines (Fund for the Replacement of Animals in Medical Experiments, FRAME) to research the alternatives to animal models for the study of passive transfer. No suitable alternatives were found by this method.

Why were they not suitable?

The study of passive transfer from mother to calf cannot be replicated sufficiently through the use of either cell lines or organoids, especially given that the underlying physiology is multi-organ and not limited to a specific tissue or cell type. Study of maternal effects are not possible via these methods. Validation of a lateral flow device for antibody measurement requires animal disease models.

Reduction

- Sample sizes were estimated using standard power analyses based upon our pilot data.
- Taking into account the results of a pilot study (unpublished) of 16 farms within Southern England, and through collaboration with a veterinary practice, we considered the effect of farm selection on risk of losses to follow up and prevalence of disease to ensure selection of an appropriate farm that meets the requirements for this project.
- We will use residual blood samples wherever possible, already routinely collected under the Veterinary Surgeons Act (VSA) for the purpose of measuring mother metabolic and health status pre-calving, and for measurement of calf health and immune status (with permission from our Clinical Research and Ethics Review Board).

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

- CliniĻH

The study outcomes of the project are only relevant to cattle, and are specific to their immune development during pregnancy and during the neonatal period. Due to its complexity, animal models are the only available method and there are no less sentient species that can be used for this research.

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

Animals will be handled by trained operators in a manner that avoids prolonged handling and minimises stress, either in their housing environment or using appropriate handling facilities. Study animals will be monitored for signs of adverse effects associated with venepuncture during subsequent visits. Risks will be minimised by use of a sterile needle for each collection of the smallest practical gauge. In circumstances where the collection site is dirty it will be cleaned prior to sampling

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

Published practical guidelines are available to us to ensure that the design, collection of data and reporting of our scientific findings are clear, repeatable, and legitimate. These guidelines are variable depending on the type of study which we report. Since this project licence covers a number of potential publications, there are various guidelines which we will follow. For each guideline mentioned, further information is accessible via the hyperlinks provided.

For example, during the experimental planning and design stage we have followed the PREPARE guidelines (provided by Norecopa), which provide clarity on how to ensure this stage of our research is optimised.

During the project reporting stage of the project, we will follow the ARRIVE 2.0 guidelines. We will also consider the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and, for comparison of diagnostic tests, the Studies of Diagnostic Accuracy (STARD) guidelines when writing for publication to ensure transparent experimental design and clear reporting. Each one of these guidelines provides the authors with specific advice relevant to the study design which we intend to report.

https://norecopa.no/prepare/

https://arriveguidelines.org/arrive-guidelines

https://www.strobe-statement.org/

https://www.equator-network.org/reporting-guidelines/stard/

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?

This institution is active in the dissemination of NC3Rs and 3Rs relevant news and training via a newsletter and regular group meetings, which I will participate in.