

NON-TECHNICAL SUMMARY (NTS)

Project Title	Studies to investigate laminitis predisposition
Key Words	Horse, laminitis, endothelium, insulin, metabolic
Expected duration of the project	5 year(s) 0 months

Purpose of the project (as in ASPA section 5C(3))

Purpose	
No	(a) basic research;
	(b) translational or applied research with one of the following aims:
Yes	(i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants;
No	(ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants;
No	(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes.
No	(c) development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the aims mentioned in paragraph (b);
No	(d) protection of the natural environment in the interests of the health or welfare of man or animals;
No	(e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work;
No	(f) higher education or training for the acquisition, maintenance or improvement of vocational skills;
No	(g) forensic inquiries.

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):

The objectives of the project are to:

1. Investigate methods to assess the function of the endothelium (blood vessel lining cells) in the whole animal

2. Study the effects of season, diet and exercise on markers of abnormal endothelial function to determine whether the release of these markers is different between normal and previously laminitic animals.
3. Study the role of microparticles (microscopic cell particles) in abnormal equine endothelial cell function in the laboratory
4. Study the effects of short term feeding of various feedstuffs at different times of the year on metabolic responses, fat tissue gene expression and faecal bacteria in normal and previously laminitic ponies to determine whether differences are present which could be used to identify susceptible animals.
5. Undertake a prospective study to identify whether metabolic alterations occur prior to disease onset which could be used to identify susceptible animals.

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)?

The potential benefits likely to derive from this project are an increased our knowledge of the role of abnormal endothelial function, inflammation and insulin in the pathogenesis of laminitis which may allow treatments and prevention strategies to be devised. In addition, by increasing our understanding of why certain individuals are predisposed to laminitis, animals at risk could be identified and preventative management countermeasures instigated in a more effective manner. These benefits they will hopefully lead to a reduction in the frequency of occurrence of this extremely painful equine condition and to improved treatment strategies. which in turn will have a significant impact on equine welfare.

What types and approximate numbers of animals do you expect to use and over what period of time?

Adult horses will be used in this project. The majority of studies will use a maximum of 15 previously laminitic and 15 non laminitic animals over 5 years. Up to 400 not previously laminitic animals will be used in a single prospective study conducted over a 4 year period.

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected levels of severity? What will happen to the animals at the end?

- The possible adverse affects include anaemia and thrombophlebitis associated with blood withdrawal, collapse following sedation, wound infection in conjunction with fat tissue biopsy, exhaustion associated with over exercising and laminitis following excessive carbohydrate consumption.
- The likely/expected level if severity is mild.
- At the end of the majority of studies, animals will be inspected by the named veterinary surgeon to determine whether the animals are suitable for continued use in another protocol under this or another project licence, to be kept alive at the designated establishment or to be discharged from the controls of the Act for example to be a companion animal.

Application of the 3Rs

Replacement

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

Replacement

It is not possible to achieve the objectives of this project without using animals as we are studying complex metabolic pathways and physiological responses which vary with daylight length and season that cannot be modelled using isolated tissues, cells or computer simulations.

Reduction

Explain how you will ensure the use of minimum numbers of animals

Reduction

Group sizes of up to 30 animals will be used in the majority of studies. This is in keeping with group sizes that appear in many publications using similar experimental designs. On each occasion, we will use the least number of animals possible to provide reliable and reproducible results based upon the experience of the researchers and evidence from published literature.

The proposed number of animals to be used in the prospective study has been discussed with epidemiologists and statistical calculations have been performed to ensure that the minimum number of animals is used.

Refinement

Explain the choice of animals 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.

Refinement

Laminitis is a disease which affects horses and ponies and it is therefore most appropriate to undertake these studies in equidae. The unique anatomy of the equine foot and the precarious balance of forces in the blood supply to the foot of this species are central to the pathophysiology of the disease. Thus, our studies to further elucidate the role of insulin resistance, inflammation and abnormal endothelial function in the pathogenesis of the disease require experiments using whole animals. Whilst we can model some aspects of the disease in the laboratory, ultimately, methods to identify laminitis prone animals have to be tested in experimental horses and ponies (both control and previously laminitic animals) before moving to interventional field studies.

The welfare costs to the animals involved in the project will be minimal as all of the proposed studies are mild and the likelihood of adverse effects is very uncommon.