A validated experimental model of *Mannheimia haemolytica* infection in calves

Introduction

Acute bovine respiratory disease (ABRD) is a complex infectious disease and one of the most common causes of morbidity and mortality in calves.

Non-infectious predisposing factors include stocking density, poor ventilation, stress and mixing of calves from different sources or of different ages.

Infectious predisposing factors include viral and bacterial pathogens. The main viruses are: respiratory syncytial virus (RSV), parainfluenza type 3 (PI3) virus, infectious bovine rhinotracheitis (IBR) virus and less obviously bovine viral diarrhoea (BVD) virus. *Mannheimia haemolytica* is one of several bacterial species which can be involved some others being *Mycoplasma bovis, Pasteurella multocida* and *Histophilus somni*.

Moredun Scientific offers a validated experimental model of *M. haemolytica* infection in calves for use in client studies to test the efficacy of novel vaccines and therapeutics. The model has been used successfully in both vaccine[1,2] and antibiotic[3,4] therapy trials.

Model Overview (Vaccine studies)

Vaccinated and control animals are challenged with an *M.haemolytica* isolate on a single occasion. For four days post final challenge, the animals are clinically observed at which point the animals are euthanased and the lungs assessed for the presence of *M. haemolytica* specific lesions.

Challenge Model

The strain of *M.haemolytica* used in the model was isolated from cattle with clinical respiratory disease in the UK. This isolate has been used in a number of different client studies with considerable success.

The growth of this isolate has been fully validated using defined growth media and conditions and the production of challenge material to a defined level is reproducible within tightly defined limits.

The model is a high volume, low concentration challenge, which limits the potential for immediate endotoxic shock in animals (by reducing the number of bacteria present in a location and therefore the concentration of endotoxins) and provides a good spread of the organism within the lungs.

Clinical Signs

A critical aspect of *M.haemolytica* studies is to ensure a consistent challenge success rate. The Moredun model, which utilises endo-bronchial deposition of a low volume/high titre challenge on a single occasion, has been shown to be effective with typically 80% of challenged animals showing clear signs of respiratory disease within a four day period post challenge.

The model has been validated to produce clear signs of clinical disease including increased rectal temperature, increased respiratory effort/rate and poor demeanour. Figure 1 shows an example of lung lesion scores following challenge in a vaccine study.

Lung Pathology

The main determinant of the efficacy of the challenge for the majority of studies which use the Moredun model is the percentage of total lungs with lesions. The mean % lung damage in the control groups is generally 15 to 20% and significant differences between treated and control groups are routinely observed.

Bacteriology

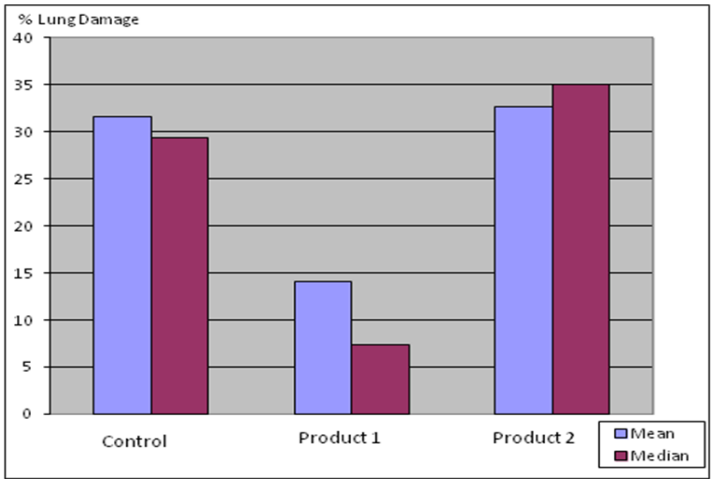
The presence of the challenge isolate in the lungs of study animals is confirmed by recovery of the bacteria from lung tissue samples collected at necropsy.

Homogenised samples are titrated onto blood agar plates for accurate colony counts. Colonies consistent with challenge are recovered in large numbers from all challenged control animals.

The *M.haemolytica* model is one of a portfolio of validated experimental models of respiratory disease available for efficacy studies for vaccines and therapeutic agents.

We have GLP accredited animal and laboratory facilities and independent Quality Assurance department to ensure all studies are conducted to the required quality standards.

Figure 1: Lung Lesion Scores (Weighted)



Contact Us

Email: info@moredun-scientific.com
Tel: +44 131 445 6206

Moredun Scientific
Pentlands Science Park
Penicuik
Near Edinburgh
EH26 0PZ
Scotland, UK

References

1. Crouch *et al*, Vaccine 2012, 30 pp2320-2328
2. Makoschey *et al*, Vaccine 2012, 30 pp969-973
3. Achard *et al*, Vet Record 2018, http://dx.doi.org/10.1136/vr.104795
4. Forbes *et al*, Antimicrobial agents and chemotherapy, 2011, 55 pp831-835