A validated experimental model of *Actinobacillus pleuropneumoniae* respiratory infection in pigs

Introduction
The bacterium *Actinobacillus pleuropneumoniae* (APP) is a Gram-negative coccobacillus and the causative agent of porcine pleuropneumonia, a contagious disease of major economic importance in the pig rearing industry worldwide.

The organism is carried in the lungs and upper respiratory tract and generally affects pigs of 8-16 weeks of age. Infected pigs may develop acute haemorrhagic-necrotising pneumonia and fibrinous pleuritus or chronic localized lung lesions and adhesive pleuritis, resulting in reduced finishing weight and possible death. There are a number of different serotypes of APP some of which are highly virulent.

Moredun Scientific offers a validated experimental model of APP infection in pigs for use in client studies to test the efficacy of novel vaccines and therapeutics[1].

Model Overview (Therapeutic studies)
Pigs are sourced from farms with no known history of APP infection. At between 5 and 6 weeks of age the animals are challenged intra-nasally with an APP isolate. The animals are clinically observed and enrolled on the study up to 12 hours post challenge once clinical signs of respiratory disease are observed.

Post enrollment clinical observations are carried out daily for 4 days at which point the animals are euthanased and the lungs assessed for the presence of lesions. Lung tissue samples are collected from specific sites and cultured to confirm the presence or absence of the challenge organism.

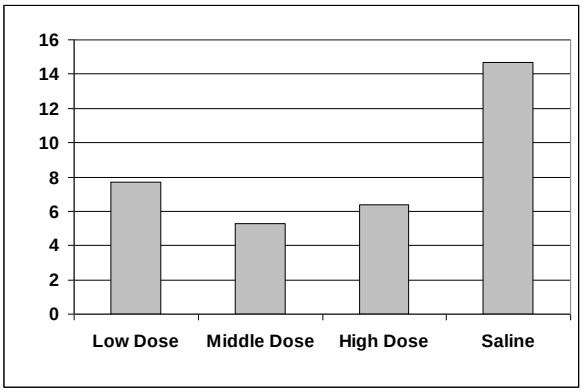
Clinical observations consist of rectal temperature and assessments of demeanour, type of respiration, coughing and body condition according to a scoring system.

Challenge Model
The strain of *APP* used in the challenge is a Serotype 9 field isolate from an outbreak of porcine pleuropneumonia. The growth of the 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.

Clinical Signs
The model has been validated to produce clear signs of clinical disease including increased rectal temperature, increased respiratory effort/rate and abnormal demeanour. These clinical signs allow enrollment of animals on therapeutic trials based on clearly defined and validated

criteria. The standard design for enrollment requires animals to have an increased rectal temperature and either abnormal demeanour or respiration. Figure 1 shows an example of typical clinical scores from a therapeutic study.

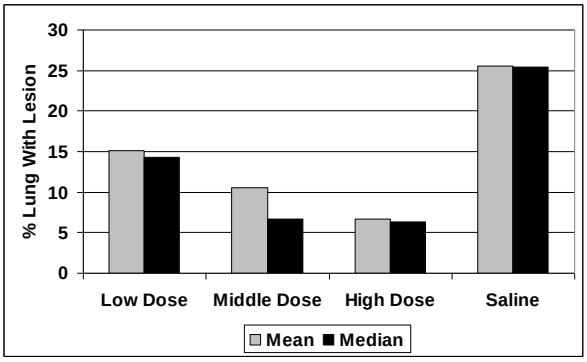
Figure 1. Summed group total clinical scores



Lung Pathology

The main determinant of the efficacy of the challenge is the percentage of total lungs with lesions. The mean % lung damage in the control groups is generally 25% and significant differences between treated and control groups are routinely observed. Figure 2 shows an example of lung lesion scores following challenge in a therapeutic study.

Figure 2. Lung lesion score per treatment group



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 with samples titrated onto chocolate agar plates for accurate colony counts.

Serology

Serum samples are collected on Day 0 and at necropsy and analysed for the presence of antibodies to *A. pleuropneumoniae* serotypes 1 to 12 using a commercially available ELISA kit.

The APP model is one of a portfolio of validated experimental models of porcine disease available for efficacy studies for vaccines and therapeutic agents.

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

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Reference

1. Thomas *et al*, European Society of Porcine Health Management 2012.