ELLEGAARD
GÖTTINGEN MINIPIGS

Welcome to the webinar:

Refinements in Minipig Inhalation Toxicology

26 October 2021

Guest speaker: Alice McNamara | Labcorp, UK

- Many have signed up for this webinar from around the world and therefore all attendees are muted to avoid background noises, delays in sound, echoes etc.
- Please ask your questions in the questions/chat section and we will follow up in the Q&A sessions following the presentation.
- We encourage everyone to complete the survey after the webinar, so we can continue planning relevant, educational, and insightful webinars.
- Presentation slides and a recording of the webinar will be shared within 1-2 days via email.
- For certificates of attendance, please complete the survey following the webinar.

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Alice McNamara

Refinements in Minipig Inhalation Toxicology

26 Oct 2021

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Refinements in Pig Inhalation Toxicology

Overview

- Why inhalation?
- Why pigs?
- Challenges
- Refinements
  - Training
  - Physical environment
  - Safety monitoring
- Future

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Why Inhalation Toxicology?

Safety assessment

- Clinical delivery of respiratory pharmaceuticals, e.g.:
  - COPD
  - Asthma
  - Cystic fibrosis
  - COVID
- Clinical delivery of systemic pharmaceuticals, e.g.:
  - Multiple sclerosis
  - Migraine
  - Parkinson's
  - Anxiety
- Unintended exposure during manufacturing, handling or use of chemicals and agrochemicals

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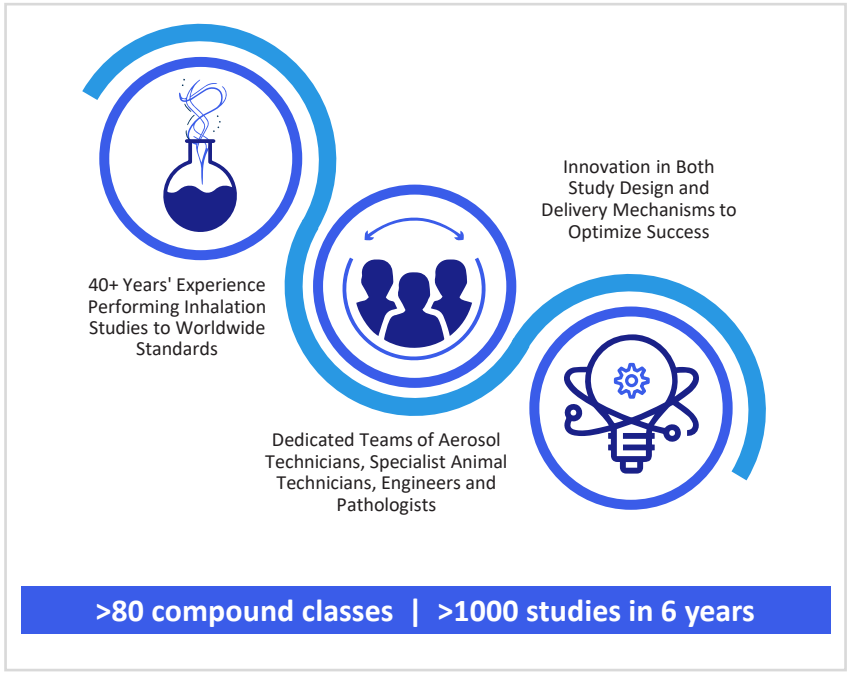
Inhalation Toxicology

Our capabilities:

- Acute to carcinogenicity
- Embryofetal to two-generation reproductive studies
- Studies with specific approaches and dosing up to 24 hours/day
- Cardiotoxicity to assessing anesthetic potential

- All work is performed in accordance with the Animals (Scientific Procedures) Act 1986 (amended in 2012 to conform with European Directive 2010/63/EU)
- Ethical review of all project licences by internal Animal Welfare and Ethical Review Body and UK government Animals in Science Regulation Unit



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Why Minipigs?

Ethical factors

Scientific factors

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Challenges

- Developing background data
- Pig welfare (and compliance)
- Equipment
- Pig safety

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Developing Background Data

Respiratory plethysmography

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Pig Welfare (and compliance)

- Working with conscious pigs is essential to allow 1 hour+, repeat dose inhalation exposure in large numbers of pigs
  - Welfare
  - Replication of intended dose routes
  - Efficiency
- Training
- Environment
- Equipment

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Training

- 28 day+ training programme
  - Longer doses need longer training periods
- Socialisation in pen
- Harness and lead training
- Walking to dose suite, feeding treats from mask
- Bench restraint
- Mask with air
  - Slow escalation to eventual dose length

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Key Training is Before Mask

Animals walk voluntarily to dosing suite

- Create positive associations with:
  - Staff
  - Harness
  - Dosing suite
  - Mask

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Animals will voluntarily walk onto dosing “bench”

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Physical Environment

- Transport
- Dose suite
- Mask

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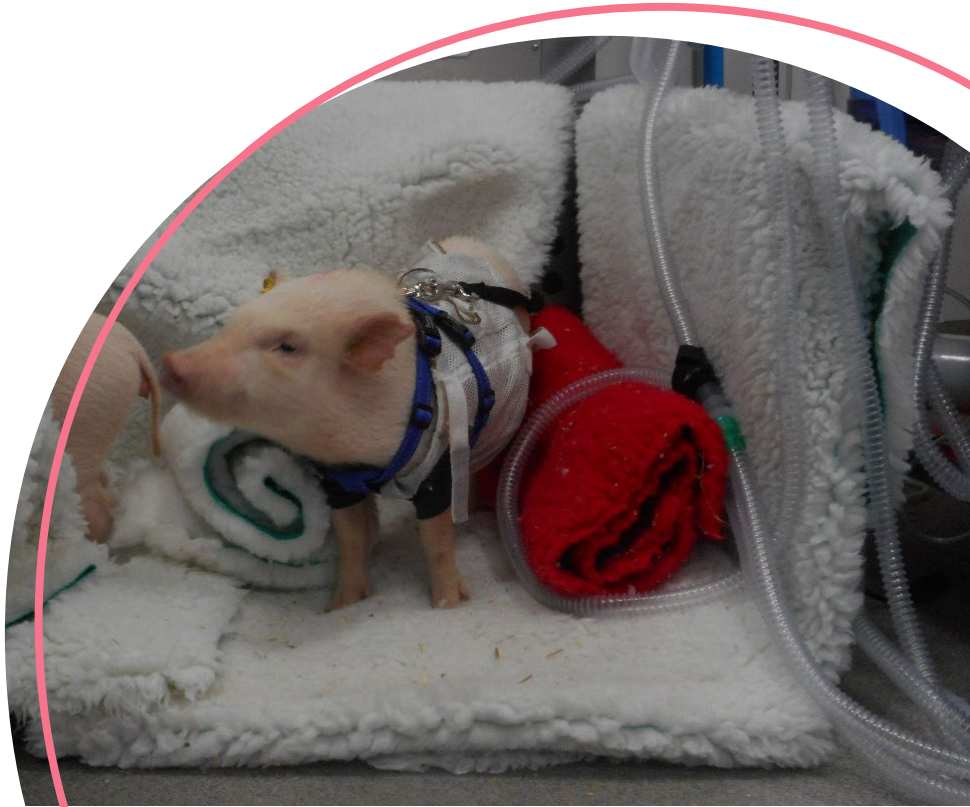
Dose Suite

Optimizing the room for pig dosing

- Consistent
- On floor
- Surface substrate
- Quiet but not silent
- Light levels
- In groups where possible
- Comfort bolsters
- Every pig is different



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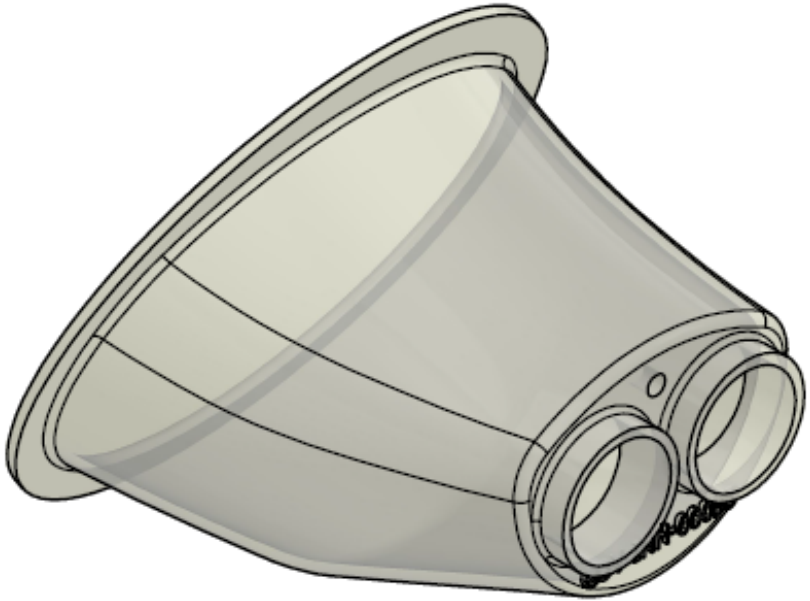
Computer-Aided Design and 3D Printing



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Masks in Use

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Safety Monitoring

- Constant supervision
- Behavioural scoring
- Capnography

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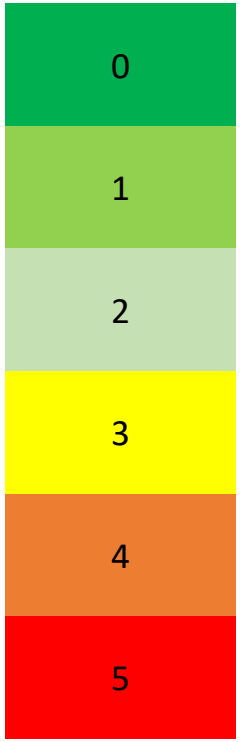

No observation of aversive behaviours, e.g., trying to remove mask or leave bench

Occasional observation of aversive behaviours, e.g., trying to remove mask or leave bench

Occasional to intermittent observation of aversive behaviours, e.g., trying to remove mask or leave bench

Intermittent observation of aversive behaviours, e.g., trying to remove mask or leave bench

Intermittent to repeated observation of aversive behaviours, e.g., trying to remove mask or leave bench

Repeated observation of aversive behaviours, e.g., trying to remove mask or leave bench

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Capnography provides real-time data about respiratory rate, depth and quality

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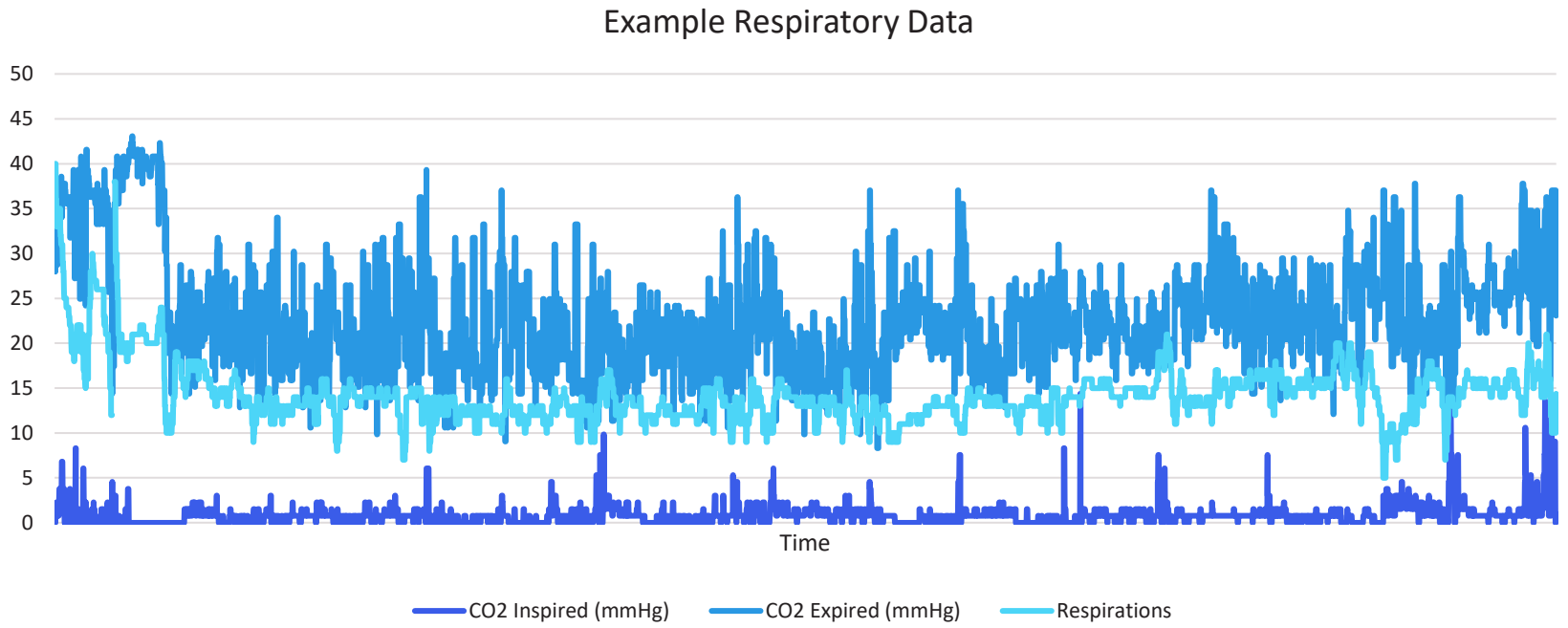

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Future

- Constant cycle of refinement
  - Technician-led AWERB subgroups for dose route (inhalation) and species (minipig)
- Longer term studies
- Different study types, e.g., dose modalities

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Thanks to all the staff at Labcorp Huntingdon who have collaborated on this project, including:

Dog & Minipig Toxicology team

Aerosol Technology team

Inhalation Engineering team

Cardiovascular Safety Pharmacology team

Study Management team

Animal Welfare & Veterinary Services team

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