

Refinement of Minipig Inhalation Restraint Training

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Introduction

Minipig inhalation is a novel procedure. In previous years, our Labcorp Huntingdon site has performed validation work for minipig inhalation, but only in the last year have we been able to offer minipig inhalation studies as an option to our customers. We have now successfully performed a 32-pig study for regulatory submission, as well as several preliminary studies, and are expecting several more by the end of the year. We are currently the only CRO that is offering this model. This allows scientific flexibility for sponsors to select the most appropriate species, based on the action of the test article. Under UK law [Animal (Scientific Procedures) Act], dogs and nonhuman primates should only be used when no other species is appropriate, so using minipigs where possible is a relative replacement.

Methods

Due to the increase in demand to complete more minipig inhalation studies we looked to refine this procedure further. This would allow improved animal welfare and increased animal compliance with the procedure. This refinement included every aspect of the dosing procedure, including changes to mask design and the inhalation system itself, as well as a large focus on training, led by the Animal House. This included:

- Positive reinforcement
- Habituation to human contact
- Harness training
- Lead walking to dose suite
- Sham dosing
- Environmental enrichment of the dose suite

Our first thing to look at was the length of time we used to train and get our pigs used to being placed in harnesses and walking to the dose rooms. Pigs do not enjoy being picked up, so having the animal trained to walk to the room reduced stress for animal and staff alike. Animals need to be lightly restrained on the benches and comfortable enough to lay calmly in the dose room for a variety of lengths of time depending on the study design. This requires an extended period of training, where animals are sham dosed with air for increasing lengths of time. For example, the design for a recent study required us to dose for 120 minutes. From previous experience, it was decided to reduce the gaps between the time increments that we standardly use for canines and limit the gaps to 15-minute intervals with 2 days at each time period so we could train the pigs to comfortably relax during the dosing periods.



To ensure the pigs could be comfortable enough to for the full periods of dosing, it was found the standard offering of a sheet of vet bed on the bench (that canines are very comfortable with) didn't suit the pigs. Each pig seemed to have different requirements. During the first few days, we needed to see what each one preferred; from rolled up vet bed positioned under their heads, to layered vet bed to raise them up to a higher position. Some prefer facing downwards and some looking up. This method benefited from the decision to use as much of a same team as we could each day so the technicians could understand and recognise the different behaviours displayed by individual pigs.

To ensure we could build up a positive relationship between the pigs and the technicians, we started getting close to them from very early on when they arrived. We achieved this by spending time in the pens with the pigs, offering fruit by hand and giving them Actimel® via a syringe. We do this for the first 14 days after arrival as standard practice, and it helps build a very positive rapport. Once the 14 days are up, we then switch to blackcurrant to continue the bonding process. During this time, harnesses and vet bed would be introduced in the pens to get the pigs used to it.



Result

Due to the reactions pigs have when handled, we made sure to put harnesses on while the pigs were on the ground to reduce any stress at the beginning of the procedure. By using fruit rewards and repetition, the pigs got used to walking to the dose suites and stepping onto the benches, ready to be restrained for dosing.

We have completed a number of studies up to 28 days in duration and up to 40 animals per study, but continue to refine this with the dedicated animal operation team.



With these alterations, we feel we are moving forward in making this procedure better for the pigs and the staff. We are continually looking at our training to make any improvements we can.

The work is conducted under UK Project Licence, which has ethical approval from AWERB in an AAALAC-accredited facility.

