Royal Veterinary College
University of London

Summary Minutes: AWERB: PPL Review meeting

Status: FINAL

Meeting held: 10 April 2024 at 2.30pm via MS Teams

Present: 12 plus 1 in attendance, 6 by invitation and 16 apologies

1 WELCOME

A new member was welcomed to her first AWERB meeting. She was in training to become a NACWO.

2 AMENDMENT TO PROJECT LICENCE

The project licence holder (PPL Holder) and a colleague were welcome to the meeting. The PPL Holder explained that he was seeking to make an amendment to add a new species to the licence, as he had been advised by regulators that this might be required in order to confirm that the viral vectors being used were safe prior to proceeding to clinical trials in humans.

Several queries were raised by AWERB, primarily in ensuring that the maximum volumes being used was made clearer and also how the injections would be given.

It was noted that although the licence referred to scruffing rodents to aid the collection of urine, this would be changed, as a new method had been devised involving a collection tray being placed at the bottom of an empty cage to collect the urine.

AWERB sought clarification whether the injections would be into one or two kidneys as the licence mentioned that the injection would only be into one kidney, but then later it was implied that it was into two. It was confirmed that currently it was just the one kidney for the echo guided injection to make sure that it was safe.

The PPL Holder and his colleague were thanked for attending the meeting. Once the requested amendments had been made to the licence, it would be circulated for a final review.

3 NEW PROJECT LICENCE APPLICATION

The project licence holder and colleagues were welcomed to the meeting. It was explained that this was a new project licence application, and the PPL Holder would be attending a PPL Training course shortly. The work was currently being done under an existing licence but as that PPL Holder was retiring, it had been decided that a new licence should be written. Their research focused on respiratory research, in particular developing new compounds designed to treat either basic chronic diseases or to use as anti-viral drugs.

The following questions were raised:

- *One of the humane endpoints mentioned laboured breathing, with the rodents being euthanised after 6 hours if there was no improvement. AWERB were concerned about the length of time that a rodent could be left struggling with laboured breathing, as this would be quite distressing*

and exhausting.
The PPL Holder clarified that by laboured breathing they were referring to rodents that had been dosed and were noticeably making a bit more of an effort to breath but that this generally resolved itself pretty quickly; this was different to the next category which was abdominal breathing which involved a continual effort to breath hard, resulting in their posture being slightly hunched to help with the effort of breathing. For that type of breathing if there was no improvement after 10 minutes, then the animal would be euthanised. The explanation of what was meant by laboured breathing would be added to the project licence.

The six hours had been decided on as it was feasible that an animal could spend a longish time showing a difference from normal in breathing between dosing, even though the effect of dosings might be quite mild. Having this time period provided plenty of opportunity for an animal to recover.

- *The licence mentioned that an animal could be anaesthetised once a day for up to 28 days. Was that typical? Although the procedure might be minor (less than 5 minutes) it could still lead to a cumulative effect?*
  This would not happen very often. When they had previously carried out intensive studies, there had been no signs of adverse effects from the inhalation anaesthesia with the animals recovering quickly and showing no aversion into going back into the chamber. A sentence would be added to the licence to confirm that stringent checks were made to check that the animal was healthy and suitable to continue receiving the procedure.

- *The licence mentioned that where discrete venepuncture was used, up to 8 samples could be taken in any 24hour period. This seemed to be a lot. Was the same site used? Also if up to 8 blood samples per day were being taken then a check would need to be done on the blood sampling volumes that were allowed to be taken to make sure these were not exceeded.*
  The licence would be amended to follow NC3Rs guidelines of up to 4 samples per 24 hour period. A check would also be done to ensure that LASA good practice guidelines were not exceeded.

- *Oral dosing: the licence mentioned that there could be food withdrawal of up to 18 hours which was a long time to withdraw food from a rodent. It would also affect the body weight, which was one of the monitoring regimes, so would result in body weight issues. The normal gastric emptying time for a rat was approximately 6 hours. Why was 18 hours needed?*
  it was explained that with studies due to start at 9am, food withdrawal of 6 hours was not practical. It would also be very costly to pay staff to come in during the middle of the night to withdraw the food. Historically 18 hours had been agreed with the Home Office as an acceptable level for the food withdrawal. AWERB argued though that 12 or 13 hours would be more reasonable and better for the animals. As an alternative were automated food feeders that "closed" on a timer an option? Another option could be to change the dosing time to later in the day, so the rodents could be starved from the morning. It was agreed that information would be obtained on the impact of different timings on food withdrawal, to determine the best practical approach for the study, the animals and their welfare.

- *The licence mentioned that urine and faecal samples would be collected for analysis during the project, which would either involve the animals being placed in metabolic cages for up to two days at a time or individually housed in normal cages. Was there a scientific need to collect two days' worth of data as two days was a long time for the rodents to be then reintroduced into their group, as this should be added to the licence?*
  There would be occasions when this would be required, for example when looking at excretion of a compound that had been dosed. However, where possible they would not use the metabolic cages to collect samples.

- *For monitoring food and water intake would the mice be individually housed or would the monitoring be done in groups? If done in groups how would the monitoring be done?*
  A lot of the time the animals would have been dosed the same, so the whole group would be monitored to see if there was an overall drop in food intake etc. If this happened, then the animals would be individually housed so this could be investigated further. This would be added to the licence.

The PPL Holder was thanked for attending the meeting. The licence would be revised to take into account the comments made which would then be recirculated for review.

4 **MINUTES**

The minutes of the meeting held on 05 March 2024 were confirmed as an accurate record.

5 DATE OF NEXT MEETING

This was scheduled for 23 April 2024 and would be a standing agenda items meeting.

Secretary
22 April 2024