Royal Veterinary College
University of London

Summary Minutes: AWERB: PPL Review meeting

Status: FINAL

Meeting held: 6 December 2023 at 10am via MS Teams

Present: 14 plus 3 in attendance, 6 by invitation and 3 apologies

1 NEW STUDENT REPRESENTATIVES

Two new student representatives were welcomed to their first AWERB. They had applied to the recent call for new student members and were attending as observers.

2 STUDY REQUEST DISCUSSION

A request to extend an existing study had been received. It related to novel platform technologies that were being developed as part of the minimally invasive surgery markets. A new imaging and visualisation platform to improve image navigation and guidance in laparoscopic surgery was being developed. It was noted that the proposed work was very ambitious, with different streams of work being carried out in parallel. Queries were raised whether the work programme was feasible in the time scale and what would happen if elements did not work. If the programme went ahead the logistics would need to be carefully considered. AWERB concluded that before a decision could be made, more information on the study design and study plan was needed, including a scientific justification for the requested numbers.

3 NEW PPL APPLICATION:

The project licence holder was welcomed to the meeting. An application was being submitted for a new licence to replace an existing one, which was due to expire. The work related to coronary artery disease, a leading cause of adult mortality and chronic ill-health world-wide. The aim of the work was to determine which VEGF-regulated genes, VEGF receptors and components of VEGF signalling pathways were important for regulating angiogenesis atherosclerosis, cardiovascular development, and cardiac regeneration using a variety of agents (genes, proteins, shRNAs, drugs, stem cells etc) in relevant models.

There were several changes between the existing licence and the new one:

- embryo models of development would be used to observe transgenic embryos that were expressing a transgene.
- Another area of interest was repair and regeneration: they would be using a laser microscope to enable observations of real-time interactions between cells to see how they repaired.

Several queries were raised including:

- **The licence mentioned that mice would be monitored and the lesions scored: how frequently would this be done? The mice would also be weighed weekly: was that frequent enough though to pick up weight loss?**
  The lesions would be scored on a daily basis and if necessary a topical cream would be applied. The weighing would be changed to three times per week.

- **The mice would be given tamoxifen, which as that might lead to hyperglycaemia, a glucose supplement would be provided if needed. The licence also mentioned that there would be blood samples taken, which could be preceded by food being withheld for up to 16 hours. Was 16 hours an appropriate time to fast rodents for though? And would that have an impact on the mice in relation to tamoxifen and being on a brand new diet and weight loss?**
  The NVS advised that the tamoxifen would not be a long-term treatment and was only required to induce the phenotype. This would therefore be done at the start of the experiment and not at the same time as the change of diet. The 16 hours of fasting was based on Home Office guidance and basically referred to not having access to food overnight. The licence would be amended to include the frequency and maximum numbers of the blood samples.
- **The humane end points mentioned that if animals showed adverse effects that included lack of feeding or drinking then they would be terminated. However as the animals were not singularly housed then this would be difficult to monitor. A more defined general end point such as an individual's hydration level would be needed. The licence also included reference to terminating if the animals showed more than moderate pain – how would this be assessed though?**
  This section would be amended and would include assessments of pain such as the grimace scale.
- **For the fish that would be singly housed, would there be any enrichment provided to make this less stressful for them?**
  They would be kept in a box with dividers, and the box would have up to 24 singly housed fish in them, so the fish would be able to see each other.
- **For the tissue sampling, when would it be necessary to use the biopsy of caudal fin? Could swabbing be used instead?**
  Swabbing had been tried previously but had not been very successful. The biopsy provided a fool-proof method of collection.
- **Did the sham operation require a step in the protocol?**
  The licence would be amended to add that for the sham-operated hearts, the probe would be at room temperature.
- **The licence mentioned that 90% of the fish would experience moderate severity and 10% severe pain. In what way was it possible to differentiate between the pain levels experienced?**
  Severe pain was indicated through lack of movement by fish (so not swimming and staying on the bottom of the tank).
- **For the vascular regeneration, instead of anaesthetising the fish again, could the quantification of the size of the regenerated tissue be done at the time the fish were killed, rather than having to specifically anaesthetise the fish to do it?**
  It was carried out this way to enable the fish to be tracked at different time points. The anaesthesia was very brief (no more than 15 minutes).

The project licence holder was thanked for attending the meeting. The licence would be amended to take into account the comments received.

4 PPL AMENDMENT

The project licence holder (PPLH) was welcomed to the meeting. Amendments were needed as a degenerative intervertebral disc disease model, that mimics what happens in humans was being developed.

The changes included:

- Removing cattle as a species from the project licence, as they were no longer required, as they now had a minimally invasive solution.
- There was an addition of a new protocol to generate a model of degenerated intervertebral discs using administration of Chondroitinase ABC.

- The study would now focus on goats and sheep. The goat's vertebra shape was more similar to human's which was advantageous as it provided more representative biomechanics; however sheep were a common model for spine studies.

As it was effectively a new model that was being set up, it was confirmed that the plan was to initially start with cadavers and then potentially terminally anaesthetised animals. If that went well then it would go into a recovery model.

The PPL Holder was thanked for attending the meeting. A couple of changes to the licence were suggested. This would be done and then recirculated for final sign off.

5 MATTERS ARISING

5.1 Dog Unit

It was reported that a new study had started in the dog unit. This involved a new oral drug which was designed to reduce some of the effects of the muscle breakdown in the DMD model. Side effects had been experienced but it was not known for sure if this was related to the drug or its route of administration. Therefore it had been decided to delay progressing with the treatment to enable discussions to be held about changing the test therapeutic. More information should be available by the next meeting.

5.2 RSPCA LAY MEMBERS FORUM

This had been held on 5th December. Several AWERB members had attended. One of the presenters had given a talk on sentience in non-vertebrate species such as bees and insects. A question was raised about whether the RVC did any research that involved these species as the ethics of their use and the impact of caring for these species was something that would need to be considered. It was thought that the RVC was not doing any research into these species.

It was highlighted that one University had a 3Rs sub committee, that included 3Rs named champions and animal technicians, which was proving to be quite successful in building rapport. APHA had talked about interesting 3R developments including microchips that monitored animal temperature so that the animals didn't have to be handled directly.

It was agreed that it would be useful to have a detailed debrief at a future meeting to discuss what was presented at the meeting and what possibilities could be considered for the future.

6 MINUTES OF MEETING

The minutes of the meeting held on 8 November 2023 were confirmed as an accurate record.

7 DATE OF NEXT MEETING

This was scheduled for 20th December 2023 at 10am. This would be a standing agenda items meeting.

Secretary
12 December 2023