Royal Veterinary College
University of London

Summary Minutes: AWERB

Status: Chair approved

Meeting held: 22 September 2021 at 2pm via MS Teams

Present:
Attendees: 7, plus 1 in attendance, 2 by invitation and 11 apologies

1 **PROJECT LICENCE AMENDMENT**

The project licence holder was welcomed to the meeting. He explained that he wanted to make some amendments to his project licence including adding a new protocol to develop an optimal gene therapy expression tool in wild type mice for use in other protocols and also to add alternative injection routes and terminal procedures to all protocols.

A separate protocol for wild type mice that were not disease models was needed to confirm things such as expression in other organs and the best promoter for AAV to use. They had also added two additional models for kidney disease to see if they could use podocyte specific AAVs to cure those diseases, as well as adding additional routes of administration in case they were required. Of the added routes of administration, the most likely to be used was IP and tail vein. They might also do some echo guided injection through the renal artery, which they were receiving training on, from a specialist, who had a way of injecting AAV using echo guidance in mice. It was a longer procedure though so would not be done that often. The project licence holder was advised that if it was a long procedure and complex then this should be taken into account in the adverse events as there was more risk of complications.

The following queries were raised by AWERB:

- The breeding protocol referred to 8000 mice being the maximum numbers required. This was more than what the licence would actually use. What were the additional mice for? The project licence holder confirmed that these included all mice bred under this project, which he was confident was a reasonable estimate.

- AWERB pointed out that usually for amendments, when adding a new protocol, this was added to the end of the current list of protocols, rather than inserted part way through. The way the new protocol had been inserted, meant that it shifted the existing protocol numbering, so throwing things out if animals had already gone through the protocols. It was agreed that the new protocol would be added to the end and renumbered accordingly.

- The new protocol needed to be amended to confirm the highest severity that an animal could experience as it currently indicated that the protocol was mild, but also further on that it was moderate.

- If the highest severity for the new protocol was mild, then the clinical signs that had been included needed to be changed to mild.

- Details of the Animal Welfare Score to be used needed to be provided.

- Metabolic caging: A query was asked whether metabolic caging for up to 8 hours should be classified as moderate for the protocol? It was noted that A(SP)A guidance was that under 24 hours was typically a mild step. It sounded like the strains would be fairly mild with no negative effects of phenotype. AWERB consensus was that it was not necessary to make it a moderate protocol just because it had metabolic caging listed, however it would be remiss to say that there was no potential for adverse effects, so that should be mentioned. The adverse effects associated with metabolic caging included increased risk of stereotypic behaviour and also of aggression when regrouping the mice, though if they were regrouped in less than 24 hours, this should not be significant. The project licence holder advised that the cages would only be used when it was necessary to take accurate measurements of urine over a specific period of time, for regulatory reasons.

- A query was raised how often would urine be collected as it was unclear from the licence? One section of the licence mentioned that all the animals would have their urine checked; but some of the protocols only had it listed as an optional step, whereas others had it listed as mandatory. It was confirmed that urine would be collected from all experimental animals. The optional step in the protocols would be changed to mandatory.

- A query was asked about the control data for renal dysfunction as it was mentioned that it would be very tight. This would mean that the standard deviation for the control would be very small. Would this therefore be too strict? It was confirmed that it could be. The standard thing that they did to monitor renal health in their animals was through proteinuria as it was generally easy to pick up protein in very small amounts of urine. Clarity was requested about how renal dysfunction was defined as the licence mentioned that the control might be different between each experiment so what was classed as a reasonable range could be quite different between each study. It was explained that between mice strains the proteinuria changes were usually very low. When a mouse started to get proteinuria, it increases very fast. By using dipsticks frequently, it was possible to monitor when mice were starting to lose their renal function so they would then be watched very carefully. They also knew from their work the standard progress of the disease in each animal model. AWERB agreed that this was a better approach, for otherwise with the 3 standard deviation away from the mean approach, there was a risk that treated animals would be outside of the range and identified as having a renal problem, when in fact they were ok. The description of how they would define renal dysfunction would be amended.

- Time frames: one thing that was missing in general from the project licence was the idea of the time frames involved. From a lay person perspective it was useful to understand how long the experiments would last for and how they related to the humane end points and adverse effects. This should be included in the animal experience section setting out the typical length of time this model in this protocol would last for. Adverse effects and humane end points for one of the protocols also needed to be added.

- It was also important to provide sample size justification too. As the researchers were hypothesis testing at this stage, they should be able to do sample size calculations.

The project licence holder was thanked for attending the meeting. There were a few things that still needed to be ironed out, including discussions about the mild clinical signs and what to expect from

a mild and moderate protocol. Once the licence had been amended this would be circulated for a final AWERB review.

2 MINUTES OF PREVIOUS MEETING

The minutes of the meeting held on 8 September 2021 were confirmed as an accurate record.

3 MATTERS ARISING

3.1 Item 3: Keeping large animals at Camden – potential curriculum changes (8 September 2021 meeting)

A meeting to discuss the curriculum changes and provision made for Camden based students to have supervised access to the large animals at the Hawkshead campus was in the process of being arranged.

3.2 Item 6.4: Survey on rodent models of cancer (8 September 2021 meeting)

The link to this survey had been provided.

3.3 Item 6.6: NC3Rs/IAT Animal Technicians Symposium (8 September 2021 meeting)

Details had been provided.

3.4 Item 9: NVS report - fish (8 September 2021 meeting)

Work was being done on resolving the UV lighting issues.

3.5 Item 9: NVS report Establishment Licence (8 September 2021 meeting)

Most of the cross checking of the names on the Establishment Licence had been done.

3.6 Item 2: Change of project licence holder for hospital project licence (29 June 2021 meeting)

A new project licence holder had been identified so the project licence would be submitted for amendment.

4 AWERB – NEW APPROACH TO PROJECT LICENCE REVIEWS

It had been decided that the approach to scheduling project licence reviews should be changed. Currently PPL Holders request slots at an AWERB meeting in advance before the project licence application was ready to be reviewed. PPL Holders were advised that they needed to provide their applications at least two weeks in advance of the meeting, however it was found that this was not happening. It had therefore been decided that from now on, a slot would not be allocated until the project licence had actually been received (after having had an initial check by the NVS). As AWERB members needed at least 2 weeks to review a project licence, the project licence would be reviewed at the next AWERB meeting with an available slot, that was at least 2 weeks from the project licence draft having been received. These would be allocated on a first come first served basis.

As part of the new process, PPL Holders would only be sent the AWERB comments on the project licence, the day before the meeting, so that they had opportunity to read the comments before the meeting but be told not to address the comments until after the meeting as more may be received during the meeting, but it would give them an idea of the main points that would be raised at the meeting.

5 NVS REPORT

5.1 Condition 18 training

The NVS reported that he had recently attended the Condition 18 training workshop provided by the Home Office. They were now advising that if an incident happened it should be reported

immediately and a form submitted the same day, even if there was uncertainty that it was a condition 18. There was a 72 hours leeway but that was only to cover weekends. The condition 18 report should then be updated as investigations were undertaken. The Home Office had highlighted that submitting a condition 18 form was deemed as being compliant rather than not failing to comply with something. They would rather see the form and check that everything was being done properly rather than not see the form and find out later that a condition 18 report should have been submitted. A message would need to be sent to the PPL Holders to emphasise this.

If there was any possibility that an incident was related to a regulatory procedure they wanted to see the details.

Two of the NTCOs were scheduled to attend this training too and afterwards all three would meet to determine a practical plan on how to take this forward and what message to put out to the project licence holders.

5.2 Handling rabbit (Camden)

A handling female rabbit had recently died following complications after developing a hairball. The situation had escalated very quickly with the rabbit being off its food Friday afternoon and passing away the following morning. It was thought to be stress related. There had been 4 handling rabbits that were split into three pens: two rabbits were housed in the back pen; this rabbit had been in the middle pen and a male rabbit in the front pen. It was thought the female and male rabbit had been aggravating each other. There had been a planned mating between the two rabbits and the female rabbit had been pregnant when she passed away. It had been decided that the male rabbit would be rehomed and that in future there would only be female handling rabbits in the group, to make the group more stable. There would no longer be breeding from the rabbits.

5.3 Pony (Hawkshead)

A pony had to be euthanised following an anaesthesia. The pony was part of a group of ponies that had been bought in just before lockdown for a short term study. It had delayed though due to the pandemic, so a decision had been taken to keep the ponies out in the fields for about 18 months. The study was started recently and the pony had gone through the procedure, seemed to recover, but the following day it was not eating. The pony was closely monitored but as it did not improve, the decision was taken to euthanise it.

6 NACWO REPORTS

6.1 Air handling units at Camden:

A specialist consultant had now looked at the environmental parameters of the air handling unit. His report had not yet been received.

6.2 Replacement Teaching Pony

The pony had been returned back to his owner as his trial had not worked out. He had been a bit too flightly and strong willed to have at Camden with students that had not handled ponies before. Other avenues were therefore being explored.

7 END OF PROJECT LICENCE REPORTS (DEFERRED FROM 8 SEPTEMBER MEETING)

AWERB noted the two end of project licence reports that had been received. One of them had been returned as further information was required. It was noted that for the other project licence, some of the papers mentioned actually referred to a different project licence so it was suggested that the template should be revised to provide further guidance to the PPL Holders of the information that was being looked at.

8 DATES OF NEXT MEETINGS

- 5 October 2021: Standard agenda item meeting
- 27 October 2021: PPL Review meeting: to review licences that have been submitted by 13th October.

Secretary
8 November 2021