
Summary Minutes: AWERB PPLs meeting

Status: FINAL

Meeting held: 13 June 2023 at 10am via MS Teams and CEEED Seminar Room, Hawkshead

Present: 14, plus 1 in attendance, 3 by invitation and 12 apologies

1 WELCOME

A new NACWO trainee was welcomed to her first meeting.

2 NEW PROJECT LICENCE – REQUEST TO HAVE SECONDARY AVAILABILITY AT THE RVC

The PPL Holder was welcomed to the meeting. It was explained that the researcher had recently had a new licence granted at another institution to replace one that had expired. That licence had secondary availability at the RVC and the PPL Holder wanted to apply for secondary availability again.

The PPL Holder was working in collaboration with a company in developing catheters to deliver drugs to the brain. Their research had been ongoing for the last 10 to 15 years and the new project licence would allow them to deliver vectors (normally AAV growth vectors) and protein nanoparticles to the brain.

There was only one protocol listed in the licence. Several different species were listed but as the model was working well in sheep that was the current focus. The previous work had involved non recovery work but they were now considering progressing into recovery work. As the catheters were a lot more effective, the plan was to use them to deliver a variety of vectors, particles or proteins.

The following queries were raised:

- **How much pig work had been done?**
Only cadaver work had been done so far. Although pigs were a lot easier animal to use in relation to anaesthesia, they had not yet been used, as their growth rate would cause issues.
- **Did the regulators have a preference for which animal was used?**
The regulators would be happy with either model.
- **Was the plan to use sheep for the long term to avoid the growth issue of pigs; but to use pigs for the short term as they were the more ideal model to use?**
Yes. Both sheep and pigs have large gyrencephalic brains. As the current work would be carried out over months, sheep were needed, to avoid the growth rate issue. They wanted to use pigs for the short-term projects though because the recovery process and the anaesthesia was a lot easier on pigs.
- **The licence mentioned that female animals would be used but that these animals would be group housed for the benefit of their welfare. It was pointed out that the female pigs could not be group housed after surgery as they would fight. This needed to be added to the licence and permission obtained for the single housing of pigs.**

- **Under adverse effects there was mention that there would be dosing of novel compounds and substances but that the incidence of any toxic effects was unlikely. However under the “Animal Experience” section it stated that pilot studies would be used to check the safety of the novel compounds?**
Any pilot studies would be done in a smaller animal model first, before being carried out in this animal model.
- **What due diligence would be done in relation to the novel compounds?**
Evidence would need to be provided that the compounds had been through a number of in vitro and small animal experiments. The majority of these would relate to treating neurological compounds and so would be on programmes of research being run by companies that had already demonstrated efficacy.
- **What steps would be taken to ensure there was no accidental duplication of work of studies between the two institutions?**
Complete studies would only be undertaken at one institution - the work would not be done across both sites.
- **How did the minipigs cope with the catheters?**
They were not as placid as sheep but there was no history of them trying to scratch or chew the catheters out.

The PPL Holder was thanked for attending the meeting. The project licence needed to be revised to take into account the comments made and also the standard practices undertaken at the RVC and to also ensure that all the questions had been answered. Once this had been done it would be circulated again for another review.

It was noted that any amendments made to the project licence would also need to be reviewed and approved by the primary establishment.

3 NEW PROJECT LICENCE

The PPL Holder was welcomed to the meeting. He explained that this was a new licence to continue work that was currently done under a licence held by another PPL Holder, who was due to retire shortly. He was taking over the project licence as it related to research he was already doing on neuromuscular disorders.

It was explained that the direction of the future work would primarily involve two different mouse models:

- GSL30 mouse line
- MDX mouse

The following queries were raised:

- **Had organ-on-a-chip technology been looked into?**
The PPL Holder was familiar with this technology via published studies, but had not used them personally. Organ-on-a-chip technology though did not allow for the differentiated status of muscle nor was it suitable for studies involving orally administered drugs. This information would be added to the licence to explain that the technology had been considered and the reasons why they were not deemed suitable.
- **How would this mouse work translate to the neuromuscular disorder?**
There were specific reasons why mice would be used over other models. They were a very good biochemical model of dystrophin deficiency. Using mice first for studies enabled different therapeutic approaches to be screened in order to select those that looked the most likely to be effective.
- **The licence mentioned that drugs would be administered either via drinking water and food (to minimise any requirement for handling and also being more welfare friendly)**

or by oral gavage. What were the benefits between using oral gavage and delivery of the treatments in food and water?

It was agreed that as there were no plans on using oral gavage in the near future then this would be removed

- **If the treatment was being delivered through the drinking water, then what steps could be taken to ensure that the mice were drinking enough water to reach the required amount of concentration in the system?**

A small pilot study had already been undertaken under a previous licence to ensure that the amount of water that was drunk after a set amount of time was appropriate for the number of mice in the cage. The mice would also be weighed on a regular basis. Previous research had also shown that unless mice were diabetic, they would consume sufficient water to meet their daily needs. Although they might not drink the same amount each day, if they were being dosed for a prolonged period of time, they would consume an adequate amount of the drug as like other mammals, mice drink a standard amount relative to body weight. It could change a bit if the environmental parameters change (so for example in hot conditions, then the mice might consume more fluid) but in general the levels were pretty balanced.

The PPL Holder was thanked for attending the meeting. He would revise the licence to take into account the comments received when it would then be recirculated to AWERB for a final sign off.

4 NACWO REPORT

4.1 Camden

- The recent hot weather was affecting humidity within the unit at Camden.

4.2 Hawkshead

- Welfare barn: due to previous issues with the weather in the welfare barn it had been decided that once the current project involving pigs had finished (in 3 weeks) then no further studies would be done involving the pigs until September when the weather should have cooled down.

5 MINUTES

The minutes of the meeting held on 26 April 2023 were confirmed as an accurate record.

6 NC3RS REGIONAL PROGRAMME MANAGER

The NC3Rs regional team was being reorganised so that regional programme managers (RPMs) were no longer linked to specific institutions. Instead they would be delivering a range of activities to support the 3Rs in academic research nationally. This meant that when the RVC's current contract for a NC3Rs regional programme manager came to an end at the end of June it could not be renewed.

AWERB therefore needed to review how to maintain a similar level of 3Rs expertise once this change happened, particularly in relation to PPL reviews. It had been agreed by senior management that the budget that had been allocated for the regional programme manager role could be used to buy in 3Rs expertise on a part-time consultancy basis as well as provide a budget for training for the Ethics Committees. However there was concern in how to replace the Regional Programme Manager's expertise on AWERB and being able to identify someone suitable who could provide consultancy advice.

A meeting would be arranged to discuss potential options.

7 FIRST SUCCESSFUL IN-PATIENT TRIAL OF LIVER DIALYSIS

AWERB's attention was drawn to a press release in relation to the first successful in-patient trial of liver dialysis. This work had been underpinned by RVC expertise in large animal models. The proof of concept study in pigs using the device, had been undertaken by a team that included a RVC scientist, animal technicians and anaesthetists. This success highlighted why the RVC was involved in large animal model work as it results in treatment and devices for future human medicine as well as veterinary medicine.

8 DATE OF NEXT MEETING

This was scheduled for 28th June at 10am and would be a standing agenda items meeting.

Secretary
7 July 2023