
Minutes: AWERB summary minutes

Status: Chair approved

Meeting held: 07 July 2020 at 1pm by MS Teams

Present

Attendees: 13 plus 1 in attendance, 2 by invitation and 4 apologies

1 3RS ADVICE FOR PROJECT LICENCE APPLICANTS

A “3Rs advice for project licence applicants” pdf resource and a corresponding webpage had been produced by the NC3Rs. This resource aimed to give advice and highlight resources that applicants could use to address the 3Rs in their PPL application. It was suggested that it could be useful to send a copy of the document to researchers before they began drafting their project licence applications. It could also be a useful resource for AWERB members who were involved in reviewing PPL applications.

A webinar had been arranged for that Thursday to introduce this document, including a Q&A session.

2 MINUTES OF PREVIOUS MEETING

The minutes of the meeting held on Tuesday 16 June 2020 were confirmed as an accurate record.

3 ACTION LOG

3.1 Item 2: Project licence: update from May meeting

AWERB’s comments had been fed back. The species of animal had been clarified. For the power calculations, the data provided indicated that 95% of humane endpoints were reached after 4 weeks, so the study had been reduced to 3 weeks to avoid the severity increase. The numbers used for the calculations needed to be supplied and would be passed to the statistician to see if the data provided justified the numbers.

3.2 Item 9: 3Rs update (June 2020 meeting)

A mini bulletin in relation to 3R items for circulation was being put together.

3.3 Item 8: Tunnel handling in guinea pigs (June 2020 meeting)

An undergraduate student had been recruited for the tunnel handling study. The plan was that from October 2020 she would develop a questionnaire about the handling of lab guinea pigs and rats. A copy of the questionnaire would be sent to the BSU Manager and the technicians for them to review and suggest any additional questions. If lockdown restrictions permitted, it was hoped that the student would be able to come into the unit to do some practical work before she had to finish data collection by end of February 2021.

3.4 Item 15: Requested amendment to project licence (June 2020 meeting)

The project licence holder had provided a link to a webinar on the proposed new imaging technique. It was used to differentiate tissues and their components and was very similar to having an

ultrasound. It was very experimental imaging but no harms or side effects had been reported so the NVS did not have an issue with this being added to the licence.

3.5 Item 3: Enrichment for the dogs (May 2020 meeting)

Some of the technicians had come up with suggestions of potential toys that could be used in the paddocks that allowed the dogs to interact more. The suggestions would be forwarded to the internal experts for their input.

3.6 Item 4.1: SOP and guidelines: teaching animals (June 2020 meeting)

A copy of the draft SOP and supporting documents would be circulated to AWERB for them to comment on. This would also give them an overview of the processes that were in place for the handling animals at Camden. A deadline for comments would be provided, after which the document would be finalised.

It was noted that for Hawkshead the 3rd year students would not be coming back until January for their practical teaching. They would then have an intensive period of practical teaching in order to catch up. Was the same planned for the Camden teaching animals and if so, had there been any consideration about how frequently the animals would be used? AWERB were informed that a meeting had been scheduled for that Thursday with the anatomy department to discuss the returning of the students in September and the practicals. The biggest challenge for the anatomy department was factoring in social distancing with the student groups and how many students could be in the room at one time; and also how many sessions were needed whilst ensuring that the animals were not overused or stressed out. AWERB would be provided with an update after that meeting.

3.7 Item 4.2: Lame stud dog (April 2020 meeting)

The dog has now had x-rays which indicated he might potentially have early stage cruciate disease. It was too early to say if surgery might be required in the future, but it was not a reason to not rehome the dog as it was not a study related condition and might not develop significantly. Any potential owners would be advised though so they were aware of this potential risk.

4 PPL PRESENTATION

An application for a new project licence had been received. It was to replace an existing project licence that had expired. An overview of the aims of the project licence was provided. It was explained that the researchers were developing safe and effective methods of delivering therapy using stem cells, genes and drugs/proteins to the foetus and placenta, to reduce disability and death from congenital diseases such as thalassaemia, and obstetric conditions such as foetal growth restriction, pre-eclampsia, preterm premature rupture of the membranes and preterm birth. If successful, these therapies would transform foetal medicine and neonatal care, since currently there were no effective treatments for these conditions. Parents of affected foetuses currently had two options: to terminate the pregnancy or to continue, knowing the baby would be severely affected growing up, or may die before birth. Prenatal therapy would present a third option to these parents.

Vectors, stem cells and proteins would be studied in the lab on cells, before being used in any animals, to reduce animal numbers. Guinea pigs were being used because their placental development was the most similar to humans when compared to other mammals and rats in which pregnancy complications could be generated. The sheep would be used as a way to demonstrate safety and efficacy as they have many similarities in terms of foetal size, development and length of pregnancy to humans. Where possible, vectors, stem cells and/or proteins would be delivered using clinically relevant minimally invasive ultrasound guided injection, that reduces animal suffering. They would use implanted catheters to monitor heart rate and blood pressure continuously, which would beam the data to a nearby computer, allowing the animal to roam freely in their space.

AWERB were then invited to comment. The key points were:

- Throughout the application, there had not been appropriate consideration of a) the potential occurrence of adverse effects and b) description of humane end points. It was recommended that for each protocol the general humane end points should be reviewed; this should be followed by going back through to add step-specific adverse effects and humane end points. This would make it easier to work out what adverse effects were expected and when to apply the humane end points.
- More information was needed to enable an effective harm benefit analysis to be done.
- For general anaesthesia the licence mentioned that there would be no adverse effects, even though there were potential adverse effects that should be looked out for.
- The way the steps had been written was difficult to follow both for the reviewer and also for the people using the project licence to guide decisions during the day.
- Accumulative adverse effects needed to be taken into account. There were several different procedures taking place in the protocols, yet no mention was made about the effects of doing repeat procedures on animals.
- The weight loss of 25% in protocol 7 was a major weight loss. Justification would need to be given about why this was required.
- Reduction and experimental design: this should be included within the project licence in order to demonstrate how the power calculations had been done and why they were appropriate for each of the different protocols.
- An alternative method of administration for the IM injections should be looked into as this was a painful procedure.
- A query was raised about what was restricted in the diet that meant the guinea pigs had to be singly housed. This would be stressful for the guinea pigs. Was hybrid housing an option? Would control animals undergo the same housing conditions?
- The way the protocols were written was confusing. There was also information that should be put in the adverse effects section. The NVS would work through one of the protocols to show what was being looked for in these sections.
- Under the protocol justification: “the most refined for the section” the examples that had been provided actually related to reduction rather than refinement. It was pointed out that there were other instances in the project licence that could be used instead (such as using post injection analgesia).

AWERB noted that this project licence was a continuation of previous work. What had already been learnt from the previous research: what had been its impact? The project licence holder explained that in relation to growth restriction:

- they had taken an idea all the way through to a potential treatment and had submitted a clinical trial application to MRC for this drug, who wanted to test it out on guinea pigs, which they would fund.
- On the back of that work there was a greater understanding of how drugs work in relation to growth restriction.
- There was a whole programme dedicated to identifying which women could be selected for a clinical trial of growth instruction and why some drugs would not work;
- For stem cell transplantation – there had been in utero injection of stems cells and gene therapy which had resulted in a low complication rate for the foetus. Those data had been used to support the first human clinical trial of stem cell transplantation. Subsequently a Swedish partner have been able to treat only the second baby in the world.
- Engineers were developing novel imaging techniques to be tested in animals so that the research could be taken into clinics.

- Work had been done on trying to find where the needle tip goes – this had then been made into a clinical device, with manufacturers approached about hooking this up to their machines in order to get data to demonstrate to the safety people that it was safe.

The project licence holder was thanked for attending the AWERB meeting. AWERB would finish reviewing the licence and a summary of their main questions would be compiled for her to respond to.

5 PROJECT LICENCE AMENDMENT

A request to make an amendment to this project licence had been received. This was to allow repeat cystometry and recording up to 9 months after implant surgery, rather than the currently specified 6 months. A redesign of the amplifier and cable had been required though due to difficulties in getting clear readings due to the building of the recording equipment and interference from the surrounding area. Work on this had been delayed by reduced access to the engineering labs during the lockdown. Although work was now progressing, it would not be completed by the current deadline. An extension of up to 3 months was therefore requested to allow this equipment to be completed and further recording sessions performed to gain as much information as possible.

A general comment was made that the refinement section of the project licence did not actually relate to refinement but more about model justification. Although the project licence had already been granted, could this be amended as part of this amendment? It was confirmed that where it was identified that a project licence could be better worded or there were questions about refinement for example, the Committee could ask the project licence holder to improve these sections.

It was noted that the experimental preparations had been of a very high standard with the animals able to live relatively normal lives. The project licence holder would be asked to put together a summary of the processes and to document the refinements that had been put in place. This should then be incorporated into any papers that were written up. AWERB confirmed that they were happy to approve this amendment.

6 NVS REPORT

- **4 Pigs at Bolton's Park Farm:** one of the lame pigs had to be culled following no improvement after treatment. The delayed study had not yet been rearranged. The Chair of AWERB asked that she be notified if dates were not arranged soon as it was not acceptable for animals to be kept for a study when their welfare was being compromised.

There were no other welfare issues to report.

7 NACWO REPORTS

7.1 Camden

- **Ferrets:** there was one ferret coming to the end of the study as her body condition was slowly deteriorating and she was not performing as well in the behavioural studies as she used to do.
- **Mice:** there had been a minor issue with mice fighting in the blue section.
- **Zebrafish:** the fish group were coming in periodically to feed the fish and carrying out their licensing duties. Any health issues were communicated via a Whatsapp group.

7.2 Hawkshead

- **Rehoming programme:** this was being restarted. A proposal had been written in relation to how this could be carried out safely during the pandemic which had been approved: the main changes

that only 2 people from a family could view the puppies (instead of 4); they had to wear masks whilst on campus and had to maintain the 2 metres social distance. It had been decided that it was important to restart the programme as there was concern that other the dogs might become institutionalised.

- **Rehoming programme (general):** a query was raised about what other animals had been rehomed – these included horses; rodents (from animal handling and teaching); hamsters; handling ferrets; guinea pigs and rabbits. There were figures available on the website that detailed the number of animals that were rehomed:
<https://www.rvc.ac.uk/research/about/animals-in-research/facts-and-figures>

It was suggested that for the August meeting, an overview on the animals that were being rehomed should be given, including updates on how the animals were getting on and the feedback that had been provided which highlighted what a worthwhile programme it was.

8 NEW PPLS GRANTED BY THE HOME OFFICE

AWERB noted that there had been one project licence granted by the Home Office since the previous meeting.

9 PPLS AMENDED BY THE HOME OFFICE

AWERB noted that there had been one project licence amended by the Home Office since the previous meeting.

10 MID TERM REVIEWS OF PROJECT LICENCE

AWERB noted the mid term review that had been submitted. Work on this project licence had discontinued following one of the researchers leaving the team and the focus of the research at the Institute changing slightly. This had meant there was not much in terms of research outputs.

11 DATE OF NEXT MEETING

This was scheduled for 25th August 2020 at 10am

Secretary
13 July 2020