Royal Veterinary College
University of London

Minutes: AWERB

Status: Chair approved

Meeting held: 3 September 2019

Present
Attendees: 9 plus 3 in attendance, 7 by invitation, 10 apologies.

1 WELCOME

The Chair welcomed everyone to the meeting, including two technicians who were attending the meeting as observers.

2 NEW PPL LICENCE APPLICATION

An application for a new project licence had been received. The scientist who had reviewed the project licence to provide comments from a scientist's perspective had also been invited to the meeting.

It was explained that the researcher was applying for a new project licence to continue work that she had started at a previous institution. This had involved research on the molecular mechanisms underlying both term and preterm brain injury and resulted in the optimisation and refinement of a number of protocols and production of key papers. Her group were focussing on the efficient discovery of mechanisms underlying brain injury which occurred in babies suffering a lack of oxygen to the brain during birth and translating these discoveries into novel neuroprotective therapies. This aim could only be achieved through a considered approached which integrated *in vitro* and *in vivo* strategies to enable rapid translation to clinic.

Asphyxia (restricted blood flow/oxygen to the brain) during birth occurs in 2-3 term babies per 1000 in the UK, leading to the development of hypoxic ischaemic encephalopathy (HIE) and permanent, life-long brain and motor disorder such as cerebral palsy. Following asphyxia, there was generally a time gap of a few hours before the majority of bran cell death occurs. This time gap provides clinicians with a valuable treatment window. This project's overall aim was to identify novel therapies that would combat the devastating effects of this brain injury. The intention was to improve understanding of the cellular mechanisms underlying the evolution of the injury, so generating significant and realistic avenues for therapy development ready for preclinical testing. If successful, the project would have far-reaching, long lasting improvements on the lives of significant numbers of babies and their families. The basic science would also be of substantial interest to all researchers in the field of brain development.

The consensus view of AWERB was that the project was well written and focussed and consisted of excellent science. It was queried as to whether there were any prospects of moving the work to cell culture. The researcher explained that she was looking into a half-way house between cell cultures and animals by taking slice preparations and culturing them, a process known as organotypic culture. Once the experimentation had been done the slices would be mounted to be analysed histologically and also protein/RNA preps made from them. These experiments would inform targets for assessment in *in vivo* studies.

A query was raised whether cognitive impairment would influence the natural nursing for the new-born. AWERB were advised that the impairments that were seen were very mild. By the time a week had passed following surgery it was difficult to identify which pups had the surgery. In terms of feeding and weaning no problems had been experienced.

Once the project licence holder had left, AWERB discussed the project licence further. The main points were:

- This was an important area of research of which the committee were fully supportive.
- The harm done to the animals was relatively minor. The potential benefit from the research was huge so the use of animals was justified.
- The work being done by the researcher on *in vitro* work and brain slices was reassuring though more should be made of developing this area.

3 NEW PROJECT LICENCE APPLICATION

An application for a new project licence had been received. The scientist that had been asked to review the project licence to provide a scientist's perspective of the project licence, was also in attendance.

The project licence holder explained that the project licence would involve testing prototype devices to replace laryngeal (voice-box) functions of breathing, sound production and swallowing in a large animal model. Experiments would explore safety and potential efficacy for patients with aero-digestive disabilities.

The aim of the research was to transform the lives of those UK patients that have lost laryngeal function. Currently routine management of such cases was by patients having a tracheostomy through which to breathe and a plastic valve between windpipe and gullet through which air was passed to generate a voice. This treatment could be extremely stressful to patients though resulting in additional quality of life problems around appearance, psychology and basic human functions such as taste and smell. The intention was to test prototype devices to replace the laryngeal functions of breathing, sound production and swallowing to see if the devices were feasible and safe. Acute studies would establish the feasibility and functionality of an early prototype total laryngeal replacement (TLR) device, implanted orthotopically or in series. Acute pilot studies would also permit further optimisation of surgical techniques and refinement of peri-operative care protocols in preparation for later, recovery studies. Chronic studies would examine the functionality of an early prototype total laryngeal replacement (TLR) device, implanted in the trachea in series with the host larynx to reduce morbidity. Chronic studies would allow reassessment of the device over time and would be used to address issues of biocompatibility of the component materials that would be interfacing with the intended physiological environment. Although the materials being used have a long history of safety in clinical use, they have not been used in this particular biological environment. Recovery experiments could be extended up to six months to provide preliminary biocompatibility data prior to progressing to pre-clinical regulatory studies.

The following queries were raised:

- What was the potential for blockage? It was explained that generally there were warning signs that a blockage had occurred (such as noisy breathing) so the researchers knew that the tube needed to be taken out
- What kind of environment were the animals kept in post-operatively so that they did not damage the device? It was confirmed that the animals were individually housed but they were housed in such a way that they could see and interact with others so that they should not get stressed through being individually housed.
- What testing had the devices gone through to provide reassurance that it was likely to work when placed in the animals? There was an activator on the device that had already been

ascertained had a good level of reliability of opening and closing; the silicone used on the outside of the device was also generally well tolerated. Further testing though was needed over the inner layer of polyurethane, hence the need to supply MHRA with confidence statistics such as the outer layer not cracking.

- At what point would the research move to a clinical trial? MHRA had indicated that they needed reassurance that this device did not result in any adverse effects before it went to a clinical trial. No time period had been given for this but it provide an opportunity to refine the surgical protocol and the design of the device.

AWERB were supportive of the principles of the licence however felt more work was needed on how the licence should actually be put together. This would be done through discussions, involving the Home Office Inspector as applicable.

After the project licence holder had left AWERB discussed the licence further. The following points were made:

- This was a device that had the potential to change people's lives for the better
- The research was being done by a high quality scientific group that have had successes in the past
- Reassurance was needed about the ability to manage the animals once they have had surgery.
- It was noted that the training would be done on cadavers. A report should be provided after this training had been carried out.
- What steps were being taken to consider the mental health of the animals after the operations? What plans were there for keeping the animals entertained and engaged? It was important that they were kept in a good environment with appropriate enrichment provided. AWERB was reassured that this was standard practice for any of the animals kept for chronic studies in the unit.

4 REHOMING

The technician responsible for the rehoming scheme at the Camden campus was welcomed to the meeting. This programme focused on mice, rats, guinea pigs, rabbits and occasionally ferrets. Handling animals were bred in house and kept for a maximum of one year, before being rehomed so that they could have experience of having an outdoor life. Currently rehoming was advertised via word of mouth or through the breeding data sheets that were given to students and included details of the potential for rehoming animals.

A meeting was held with those who were interested in rehoming animals where the lifespan of the animal was explained along with husbandry routines and the required medical care. Once a decision had been made that the potential owner was suitable, the NACWO would do a check of the animal to be rehomed the day before to check that it was fit to travel. The new owner would be provided with some diet for the animal and treats that it was used to. A follow up call would be made several days later to make sure that all was going ok.

Future goals for the programme was to put together a handbook for the owners about how to settle in their new pet and tips of what to look out for in the first few days. AWERB were supportive of this suggestion.

5 MINUTES OF THE MEETING HELD ON 9 JULY 2019

The minutes of the meeting held on 9 July 2019 were agreed as an accurate record.

6 MATTERS ARISING

6.1 Action log

6.1.1 Item 3: New Project Licence Holder application (July 2019 meeting)
The project licence holder had been provided with information on systematic variation which avoided the need for duplicate experiments.

6.1.2 Item 7.1: Rat Cages – welfare project (June 2019 meeting)
This project was now underway with a month's worth of data already collected following their observations of the rats. An abstract was planned for Congress.

6.1.3 Item 11: Companion Animals Query (June 2019 meeting)
Due to the expense of obtaining a plastic pig, this was not now an option of providing an alternative companion for a lone pig. Advice was being sought from researchers that had experience in this area.

6.1.4 Item 9: Dog rehoming (April 2019 meeting)
A draft pamphlet had been put together which would be circulated electronically to AWERB for comment.

6.1.5 Item 12: Out of hours veterinary care (October 2018 meeting)
Discussions were being held with the veterinary practice that were now used by Bolton's Park Farm. A quote was being obtained**.**

6.2 Item 7: Checklist for reviewing project licences (April 2019 meeting)

AWERB reviewed the comments that had been made on the generic AWERB questions document. It was agreed that once finalised the document should be placed on the intranet. It was aimed as a check list for both project licence reviewers and also for project licence holders so that they knew the types of information/questions they should be considering when writing their project licence.

The new ASPeL system was discussed, in particular the questions that were now part of the new project licence application. There was concern that some of the questions were confusing and these concerns had been raised with the Home Office. It was agreed that when reviewing project licences, if there were questions that AWERB were unsure of, these should be highlighted and these also fed back to the Home Office.

The project licence holder's course was being updated to bring it into line to reflect the new ASPeL. These updates needed to be approved by the Royal Society of Biology.

7 NVS REPORT

7.1 Camden

A Camden visit had recently been undertaken. There were no major issues to report.

7.2 Hawkshead

Some clinical cases had been attended. There were no major issues to report.

8 NACWO REPORT

8.1 Camden

8.1.1 Condition 18 report

A condition 18 repot needed to be submitted following a mouse that had been found dead after a procedure had been done. The rest of the group of mice seemed fine. The NACWOs had no issues with the techniques used.

8.1.2 Mice

There had been issues with mice fighting. A meeting was being arranged with the project licence holder to discuss potential changes that were needed to prevent this.

8.1.3 Ferrets

The ferrets now seemed to be in the all clear following a recent virus outbreak. They were still being monitored though.

8.2 Hawkshead

8.2.1 Sheep implants

Several sheep had recently been prepared as part of the surgical procedure preparation. However the surgery has been delayed as it was found that the implant to be used had undergone manufacturing changes (change of size) that had not been anticipated. The Home Office Inspector had been contacted who had confirmed that the sheep could be returned to flock so they could be used for future projects rather than being euthanased.

9 NEW PROJECT LICENCES GRANTED BY THE HOME OFFICE

AWERB noted that there had been one new project licence granted by the Home Office since the previous meeting. The project licence had been discussed at the April AWERB meeting.

10 AMENDED PROJECT LICENCES APPROVED BY THE HOME OFFICE

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

11 STUDY REQUESTS

AWERB noted that 3 study requests had been approved since the previous meeting.

12 MID TERM REVIEWS

One mid term review had been received. A couple of queries were raised which would be sent to the project licence holder to respond to.

13 END OF PROJECT REVIEW

Two end of project reviews had been received. One provided very basic information as not much work had been done under the project licence. The second report was felt to be very thorough and comprehensive.

14 TRAINING RECORDS

All new users were set up with training folders. With new ASPeL, separate personal licence documents were no longer provided. Although it was possible to print them from the website, they were not in a very user friendly format. This had been raised with the Home Office.

15 SCHEDULE 1 REGISTER REVIEW

It was confirmed that the registers for both Camden and Hawkshead were up to date.

16 ANIMAL SCIENCES COMMITTEE

AWERB were pleased to hear that one of their members had been recently appointed as a member of the Animals in Science Committee for the following three years.

17 DATE OF NEXT MEETING

This was scheduled for 1 October 2019.

Secretary
19 September 2019