
Minutes: AWERB

Status: Chair approved

Meeting held: 10 March 2020 at 3pm

Present

Attendees: 11, plus 1 in attendance, 3 by invitation and 6 apologies.

1 PRESENTATION FROM PROJECT LICENCE HOLDER

An application for a new project licence to replace an existing project licence had been received. The aim of the project was to maintain a breeding colony of GT-knockout pigs (GTKO) in order to produce tissues for *in vitro* research which aimed to establish the basic physical and biological equivalence of GTKO compared to commercial porcine and bovine derived tissue so leading to a more fundamental understanding of the process of tissue calcification and the role of antibody in that process. The Gal-deficient GTKO pigs represented a unique resource forming the core technology needed for the development of Gal-free bioprosthetic devices. The researchers were aiming to improve the performance of replacement biological heart valves, particularly in patients under 60 years of age. If successful, the new valves would broaden the available therapies to treat younger patients, giving them a durable device that would not require lifetime anticoagulation medication so avoiding the serious thrombo-embolic risks associated with anticoagulation.

A colony of 5 to 6 animals were maintained. The animal technicians at the RVC were responsible for the breeding management and husbandry of the pigs. During farrowing, staff undertook overnight checks to ensure that assistance was available if required. The intention was to use farrowing crates to house the sow and litter during farrowing as these provided good protection for the piglets. A query was raised whether any consideration had been given to using freedom crates as these were bigger so the sow movement was not restricted? The project licence holder confirmed that she was happy to trial them but did have concerns that using them would reduce the survival rate of the pigs. If this happened, they would have to revert back to the farrowing crates as it was important to the project that piglet survival was maintained.

The animals that were produced would be sampled for DNA genotyping. Samples were generally collected through mouth swabbing. This could also be done through blood sampling by venepuncture but since switching to mouth swabbing, blood sampling was very rarely used.

A query was raised about how the existing project licence worked. The project licence holder explained that it was linked to a grant for which all the required milestones had been met. The technicians involved were excellent at monitoring and looking after the animals and their attention to detail had really made the project work. It was noted that when the project had originally been set up veterinary students had been given the opportunity to observe the behaviour of the pigs and to interact with them – was that opportunity still available? It was confirmed that the pigs were used for both student teaching and for Home Office training courses.

Further work was needed on the non-technical summary. As this could be viewed by members of the public it should be couched in layman's terms.

AWERB confirmed that they were generally content with the proposed project licence but that there were still some comments that needed to be addressed, including further work on the non technical summary as that should be couched in layman's terms. Once the changes had been done the project licence should be recirculated for approval.

The project licence holder was thanked for attending.

2 PRESENTATION FROM PROJECT LICENCE HOLDER

The project licence holder was welcomed to the meeting. It was explained that the project licence holder was applying for a new project licence to replace one that was due to expire in May 2020. The work would build upon a technique that was being developed at the RVC. Their work had found that germ-free zebrafish embryos and larvae had altered have a much more active innate immune system than their conventionally raised counterparts, while the development of the gut was retarded. This indicated that the acquisition of a microbiome was a compromise between immune and gut function. Using immunohistochemical techniques, they had identified several neuronal networks that have altered development, including the lateral line sensory system and the enteric nervous system, in germ-free embryos and larvae up to 5 days post fertilisation. This project licence aimed to explore the longer term impact of these altered neuronal networks and identify the mechanisms underlying these changes.

Several comments were raised including:

- It was suggested that as the NC3Rs Experimental Design Assistant (EDA) online tool had been used, that an example EDA diagram and report be provided to AWERB to supplement the PPL.
- It was noted that Norecopa have guidelines on zebrafish e.g. anaesthesia and analgesia of fish. There was a RSPCA/Norecopa working party report on severity classification in fish <https://journals.sagepub.com/doi/pdf/10.1258/la.2011.010181> which could be used as reference in the project licence.
- The humane end points seemed to be subjective: being based on behavioural patterns. Were there any training guidelines to help define these – for example determining when movement was faster or slower than what it normally should be? The project licence holder recognised that this was a big challenge and that it would initially be difficult to determine unusual behaviour. They had not found anything in the literature that provided advice on this – determining unusual behaviour came from experience. Their group had a tracker machine that quantified their movement and it was hoped that this work would help understand normal fish behaviour.

The project licence holder was thanked for attending the meeting and was asked to work through the comments that had been made and to then resubmit the project licence for review.

3 3RS

3.1 Pan-London 3Rs Symposium - 22nd April 2020.

AWERB were reminded about the Pan-London 3Rs symposium taking place on 22nd April. The take up from RVC researchers and technicians was very low which was disappointing. They would be encouraged and reminded to register.

The symposium programme would be covering a range of topics, including advances in organ-on-a-chip and 3D organoid techniques, impact of environmental enrichment on mouse cancer models, the

development of new technologies that can reduce animal use and improve welfare, the importance of good experimental design in developing new therapies, and harnessing big data to advance the 3Rs. There would also be a dedicated Technician Showcase Session for technicians to share their 3Rs initiatives. The closing date for registrations was 8 April 2020.

4 MID TERM REPORTS

4.1 Mid Term report 1

AWERB noted this report, in particular the concern that had been raised by one of the reviewers that although there were 9 protocols listed on this licence, only one had been used so far. The Establishment Licence Holder explained that each protocol was there to permit an individual research project to be done on veterinary patients that was not permitted under VSA. The overarching licence permitted this concept – veterinary patient studies for the benefit of research with owner informed consent. The protocols would therefore only be used, when that project was active. There were fluctuations in the level of work required particularly as and when researchers left and new researchers started.

Each time the project licence needed to be replaced, the protocols were reviewed and those that were no longer required were removed.

4.2 Mid Term report 2

AWERB had the following comments in relation to this mid-term review:

- There were several instances of the numbers of animals used and the actual severity had exceeded the originally estimated number of animals that was in the licence. [Secretary's note: upon checking the actual licence, it seemed that some of the figures in the report had been transposed the wrong way round. None of the estimated figures had been exceeded].
- Further information about the pilot studies to assess impact and severity of *Streptococcus iniae* infection and the adverse events and timing were needed to find out how this had gone.

4.3 Mid Term report 3

It was noted that no work had been conducted at the RVC under this project licence. As no work was being done here a query has been asked whether the licence should be revoked. A check was being done whether work had been carried out at the secondary availability establishment on the licence. If it had then a report of the activities that have been undertaken elsewhere was still needed so that AWERB could understand any welfare issues/3R activities etc.

5 END OF PPL REVIEW

5.1 End of Project report 1

AWERB noted the comments that had been raised by the AWERB reviewers. These had been forwarded to the project licence holder who had responded.

5.2 End of Project report 2

AWERB noted the comments that had been received on this end of project licence report, in particular that a lot of animals had been originally included in the project licence but only two types of species had actually been used. The comments had been forwarded to the project licence holder but no response had been received as yet.

AWERB were also reminded that they had reviewed a replacement project licence from the project licence holder. However, they had decided not to submit the application yet as it was not currently required.

It was suggested that for future project licence applications to replace an existing project licence, a copy of the mid-term review should be circulated with the paperwork so that AWERB were able to check whether any comments that had been made were addressed in the new licence.

6 ASC SURVEY

A request had been received from the Animals in Science Committee (ASC) to complete a survey so they could gain a better understanding of the types and frequency of communication that AWERB had with animal technician staff as they were directly responsible for animal care. RVC had completed this form and it was understood that this information would be used as a basis for a discussion at the March AWERB Hub workshop.

The Chair advised that she was very keen to encourage technicians to attend more of these meetings and she would be asking them to do presentations at the meetings about their day to day work and what it involved, as part of AWERB's responsibility was to cover animal husbandry in the unit and how they were looked after.

A query was raised whether researchers were still given the opportunity to present to technicians on their work that they were doing within the units and why that research was being done and how the work that the technicians were doing impacted on the research. It was confirmed that it was.

7 NVS REPORT

AWERB's attention was drawn to the following points:

- If an animal had to be lone housed due to a genuine husbandry reason, then there should be clear documentation in the room why this was required.
- One of the stud dogs was due to be rehomed shortly. Towards the end of last year he had a fight with a cage mate and had been lame for a few days. He improved but subsequently had recurring lameness where he would go lame for a few hours at a time and then recover. AWERB's view was requested on how much investigation should be undertaken to try and determine what was causing this. AWERB were of the consensus that investigations were needed so that any future owner could be made aware of it and what steps had been taken so they were fully aware of what they were taking on – particularly as it could also have insurance implications for the dog. It was agreed that advice from one of the Orthopaedic Surgeon's should initially be sought.

It was agreed that the rehoming policy should be amended to include this to cover this type of scenario.

8 NACWO REPORT

The following was reported:

8.1 Hawkshead

8.1.1 Berkshire pigs

Some of the new Berkshire pigs had displayed symptoms of a chest infection. This was caught very early and treated and there had been no further signs. The pigs had not yet been under protocol so were still classed as stock animals at that point.

8.1.2 Horses

5 new horses had arrived. The supplier was the first to have completed the new supplier form.

8.1.3 DMD Dogs

There had been a new round of puppies born. One of the male puppies was being hand fed as he was showing DMD propensities. Another puppy had been given food top ups but was now maintaining and gaining weight.

8.2 Camden

8.2.1 Anatomy cows:

These were being treated for ectoparasites.

8.2.2 New techniques

NACWOs would be reminding personal and project licence holders that when testing a new technique, it was important to start small and then build it up slowly to make sure there were no adverse effects.

9 CONDITION 18 REPORT

A condition 18 report had been submitted. Discussions had been held with the PIL Holder about the technique and procedure used and a training session held to provide a refresher on best practice in relation to oral gavage. The situation would be monitored.

10 SCHEDULE 1 REGISTER REVIEW

It was suggested that this item be deferred to the April meeting. This was agreed.

11 MINUTES OF MEETING HELD ON 18 FEBRUARY 2020

The minutes of the meeting held on 18 February 2020 were agreed to be an accurate record.

12 ACTION LOG

12.1 Item 2: DMD dogs (18 February 2020 meeting)

A meeting had been held with the project licence holder to discuss rehoming and breeding and putting processes in place. A further meeting would be arranged between the project licence holder and the BSU technicians to which an expert would be invited to attend so they could provide advice and make sure that what was put in place was robust.

12.2 Item 8: Condition 18 reports (18 February 2020 meeting)

An e-mail had now been circulated to PIL and PPL Holder reminding them of the process of submitting these reports.

12.3 Item 12: ARRIVE guidelines (November 2019 meeting)

There had been discussions between a couple of AWERB members about the ARRIVE question that was asked on the mid and end of project reviews and whether it should be amended so that it asked for more detail. This would ensure researchers had to provide examples of what they had done (for example randomisation or blinding had been carried out). They would be working further on this.

They had also discussed raising awareness about the ARRIVE guidelines through the PPL refresher workshops and possibly UK Reproducibility Network (UKRN) in order to encourage discussion and raise awareness that there were new guidelines.

It was suggested that this be linked into the checklist for reviewing project licences that had been provisionally drafted but not yet finalised. Consideration should also be given to the PREPARE guidelines. The checklist should encourage project licence holders to consider all of these angles.

More could also be made of the mid and end of project reviews to really probe how the project licence holders were tackling these areas.

Item 9: Companion Animals Query (June 2019 meeting)

The use of mirrors for the individually housed pig was being trialled. A report would be provided at the next meeting.

13 ANY OTHER BUSINESS

13.1 NACWO

This was the Hawkshead's NACWO last AWERB. She was thanked on behalf of AWERB for all the support she had provided with both Camden and Hawkshead BSUs, which had come along way under her guidance and care. She was also thanked for her massive contribution to AWERB and for being such a vocal member and for her work being a NACWO.

13.2 Date of next meeting

This was scheduled for 8 April 2020 at 10am.

Secretary

11 March 2020