Royal Veterinary College
University of London

Minutes: AWERB

Status: Chair approved

Meeting held: 8 January 2020 at 2pm in Camden Council Room VIDEOLINKED to Hawkshead Council Room

Present
Attendees: 12 plus one in attendance, 4 by invitation and 8 apologies.

1 WELCOME

An NTCO from an external institute was welcomed to the meeting – she was attending as part of the AWERB exchange scheme. A technician and a senior technician were also welcomed to the meeting – they were attending as observers.

2 NEW PROJECT LICENCE APPLICATION

An application for a new project licence application had been received and the project licence holder had been invited to attend the meeting. The project licence holder was involved in work whose research focus was to develop a solution to the control of *C. difficile* infection by developing new prophylactic and therapeutic treatments. The model could be used to screen a range of prophylactic or therapeutic biological interventions. The aim of this project was to enable evaluation of vaccines and oral microbiome products as a qualifying step before clinical studies.

A question was raised whether researchers would be supported in publishing any negative results that they encountered from their work? Publishing negative results was good from an animal welfare perspective, as it meant that research that had not worked was not repeated by others, but it was recognised that it was not always easy to do. The consensus was that it was possible to include negative results in papers.

There was discussion about the use of blinding and randomisation in the study. It was suggested that although the animals used would be from an accredited supplier and inbred, randomisation needed to be considered for deciding which animal went into the control group and which went into the test group. Information on whether the staff analysing the samples in the lab and carrying out the data analysis would be blinded and how that would be done was also needed in the project licence.

It was noted that for some of the experiments, only females would be used as they were generally more passive than males. Would this have an impact on when the work was translated into humans though? Was there a difference in how the infection affected men and women? The project licence holder advised that as far as he was aware men and women were affected equally. If the research progressed to the point where it could be trialled in humans, then there would be the time to ask about what would happen when put into males. At this stage although as it was not known if the approach would work, the preference was just to use females as it was less stressful to the animals. Historically though this had not been seen as an issue.

C difficile was a disease acquired in hospitals. Did this indicate that there were hygiene issues in hospitals? The “hygiene hypothesis” theory was explained in that as society now generally lived in a

super clean environment, there was not opportunity to build up immunity to microorganisms hence why gut disease had become more prominent. More should be done to make people aware of this (through public information and legislation) that it was a result of modern life style that these diseases were now so prominent and people encouraged to change their behaviour rather than relying on research involving animals to provide a cure.

The intention was to use both mice and hamsters, with the initial work being done in mice. It was explained that hamsters were considered the "gold" standard model, however mice were a lot cheaper so the preference was to do the initial work in mice and if the data generated were positive then do a follow up in hamsters in order to satisfy the regulatory bodies that the treatment worked. The model was more severe in hamsters. Thus, mice were being used as part of a triage process which was good from a welfare perspective too.

A query was raised about the intention to house animals individually in cages during the period of infection. This would have an adverse effect on the animals resulting in welfare implications that would need to be addressed. The duration of these studies would also need to be set out and added to the project licence so that a harm benefit analysis could be done. The project licence holder was of the opinion that the lone housing would likely be limited to 7 days and was prepared to stipulate that in the licence of mice but would prefer more flexibility in hamsters as sometimes onset of signs in the model took longer.

Another query was raised whether the dosage could be given subcutaneous rather than by the intramuscular route? The project licence holder advised that could be done however he would like to have the flexibility to use the intramuscular route if required though the preference would be subcutaneous. The committee were keen that the licence stipulated that the subcutaneous route would be used in preference to the intramuscular route wherever possible.

A final query was raised about the monitoring for Stage 2 as it was different: for mice it was every 2 hours, whilst for hamsters they were monitored constantly until Stage 3 was reached. It was explained that this was because hamsters developed the symptoms very rapidly so it was important that these were caught as soon as possible. There was a team of staff to provide this cover.

The project licence holder was thanked for attending the meeting. He was advised that the licence would be discussed further and AWERB would be in contact with any further queries that they may have.

Once they had left the room, the following queries were raised:

- Justification for the animal numbers was needed
- In order to assess the suitability of the substances to be administered, would in vitro work be undertaken to inform on this? What evidence would they use to inform their decision on whether to take various treatment methods forward to the in vivo model?
- For the monitoring of the animals: how many staff did they have available to do the monitoring? Was there a team of people who worked together on the monitoring so that if an animal had to be euthanased, there were still others available to continue the monitoring of the others. At what point was the decision made to cull an animal? How were the animals humanely killed?

AWERB confirmed that they were supportive of this area of research and were in principle happy with the project licence.

3 MINUTES OF MEETING HELD ON 3 DECEMBER 2019

The minutes of the meeting held on 3 December 2019 were agreed to be an accurate record.

4 MATTERS ARISING/ACTION LOG

1.1 Item 1: Project Licence amendment (June 2019 meeting)
The traffic light system document was in the process of being finalised. It would then be circulated.

1.2 Item 11.1: Animal Welfare Assessment Grid (December 2019 meeting)
Further information had been circulated to AWERB about how AWAG can help with harm : benefit analysis.

1.3 Item 11.1: Two end of PPL reports (01 October 2019 meeting)
Both reports had now been received.

5 NVS REPORT
There were no major issues to report

6 NACWOS REPORT

6.1 BSU Camden

6.1.1 **Humidity:** there were ongoing issues with the engineering: the sensors in the rooms were not matching with what the system was showing. This problem had been ongoing for some time. The company that installed the sensors no longer existed so another company needed to be identified who could look into the problems. It was noted that the issue had been raised at a recent meeting with Estates and would be raised again at the next meeting. No adverse effects on animal welfare have occurred, however.

6.2 BSU Hawkshead

6.2.1 Berkshire pigs: There had been no further complications with the new GLP study. It was not known what had caused the problems with the 2 pigs that had to be euthanased.

6.2.2 Lone pigs: A further request to use an individually housed pig had been received. This would provide an opportunity to trial several options to improve the experience for the lone pig (such as using mirrors).

7 MEETINGS

7.1 RSPCA LAY MEMBERS FORUM – DECEMBER 2019
This had been attended by two members of AWERB. A big discussion point had been the new format of the project licences and how the non-technical summaries were automatically generated from text provided in the project licence rather than project licence holders being required to write them separately. A letter with the Forum's concerns had been sent to the Home Office. This asked that, for future iterations of the project licence application, applicants be required to go back to writing the NTS themselves as it was important that researchers took the time to think about the work they were doing and why it was needed and to ensure that this was provided in lay language terms. The technical language used in the project licence was inappropriate for a NTS.

There had also been discussions about how to assess an AWERB's effectiveness. Although there was not time to discuss at this meeting it would be discussed at a future meeting.

8 3RS:

- New blog on changing mouse handling practice from an NTCO perspective https://www.nc3rs.org.uk/news/changing-mouse-handling-practice-university-establishment-ntcos-perspective#videos
- RVC would be sharing their experience through a 'tips for implementation' interview to go on the website to demonstrate the RVC's commitment and progress to this important area of global refinement in mouse handling
- New publication published on non-aversive handling (https://www.nature.com/articles/s41598-019-56860-7.pdf) specifically looking at the practicality of implementing refined handling
    - Only 2 secs handling at cage clean was sufficient to familiarise mice with tunnel handling
    - Repeated immobilisation or minor procedure (s.c.) did not reverse positive effects of tunnel handling

- International 3Rs Prize 2020 – applications for this award were now open (deadline 6 March).

  NC3Rs were looking for applications from people that have published a paper that describes outstanding and original work that has or could have major impacts on the replacement, reduction or refinement of the use of animals in research. The aim of the prize was to recognise a paper published in the last three years with demonstrable 3Rs impacts. This prestigious award consisted of a £28k prize grant and a £2k personal award.

- The NC3Rs regional programme manager had given a short presentation on her role and how she could support researchers at a departmental meeting in December.

- Experimental design – a request to help a research with an EDA diagram for a fellowship application had been received. An e-mail would be sent to all attendees of the EDA workshop held in November to remind them they could get in touch for help getting started with the EDA

- UCL had recently published a paper in Birth Defects Research which used a refined method of oral administration of tamoxifen to pregnant mice. This has been validated for efficient gene recombination (CRISPR) and has been taken up locally at UCL by other groups interested not just in lineage tracing (the interest of the paper authors) but for gene deletion (in adult mouse kidney) and also for administration to young pups – demonstrating a potential wide applicability of this technique
    - https://onlinelibrary.wiley.com/doi/epdf/10.1002/bdr2.1628

- NC3Rs grants: two grants had been submitted by the RVC for this call.

9 QUERY RECEIVED

A query had been received about whether AWERB would be supportive of a proposal to transfer animals from the RVC to a facility at another institution who were building facilities in order to house these animals.

AWERB confirmed that they were supportive in principle for the animals to be transferred. The relevant project licence would need to be amended though in order to get the authority to transfer animals between licences or to re-home with the potential for re-use under the ASPA.

10 PROJECT LICENCES AMENDED BY THE HOME OFFICE

AWERB noted that one project licence had been amended since the previous meeting.

11 STUDY REQUESTS APPROVED

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

12 MID TERM REVIEW

AWERB noted that there had been one mid-term review. Work was no longer continuing under this project licence and the project licence would be submitted for revocation shortly.

13 END OF PPL REVIEW

AWERB noted that there had been three end of PPL reviews received.

The following comments were made:

Report 1: The report seemed very reasonable. Issues had been encountered with the breeding of mice which had limited the work that could be done but the option to terminate the breeding early looked to be the correct decision. Despite these issues they had still obtained some results and had tissues to analyse which could generate further data.

Report 2: AWERB were concerned to note that no answer had been received for the 3Rs question "what, if any refinements, reductions or replacements have been introduced or identified for the future". The report would be sent back to the project licence holder to answer this question: in particular, what was being done differently under the new licence that addresses the 3Rs. If a satisfactory response was not received then the NC3Rs regional programme manager would be contacted to provide advice. The same process would be put in place for all reports now received.

Report 3: The project licence holder had developed a protocol, based on the experimental animal work undertaken, to use donor hearts from people that had died. There had been a substantial impact from this research both nationally and internationally. Their research had led to a protocol which had been used to save a few people's lives to date. The researchers were also one of the groups that really championed tissue sharing as they had been able to source hearts from a variety of other terminal surgical projects, thus significantly reducing the numbers of animals being euthanised specifically for this project. It was suggested that a case study on this project should be written on this research for the website as it was a very good example of the benefits of doing animal experimentation and also of 3Rs.

14 CONDITION 18 REPORTS

It was noted that there had been one condition 18 report submitted to the Home Office. No follow up action had been requested by the Home Office Inspector.

15 ASSESSORS LIST REVIEW

AWERB reviewed the latest version of the assessors list. There were a couple of names that needed to be removed from the list as they were no longer at the RVC.

16 FEEDBACK ON AWERB

The external NTCO was thanked for taking the time to attend the meeting. She was asked for her feedback on how the meeting went and whether there were areas that she thought could be improved. The NTCO advised that she felt the main difference between the two AWERBs related to the project licence discussion – at their meetings they went through the project licences in fine detail– whereas here it had been a more general discussion. She asked how the review of the project licences was allocated. It was explained that a core group were asked to review the licence in detail before the meeting and were also asked to lead the questioning. It was during this review that the finer details were focussed on. At the meeting, the aim was to hear more about the general aims of the project licence and approaches of the group to animal welfare and the alternatives to animal use.

17 DATE OF NEXT MEETING

This was scheduled for 11 February 2020 at 2pm.

Secretary
10 January 2020