
Summary Minutes: AWERB

Status: Chair approved

Meeting held: 27 October 2021 at 2pm via MS Teams

Present:

Attendees: 6 plus 1 in attendance, 4 by invitation and 9 apologies

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PROJECT LICENCE AMENDMENT

The project licence holder was welcomed to the meeting who summarised the changes that he wanted to make to his project licence:

- Adjustment to a protocol: addition of subcutaneous delivery of therapeutics as a possible route of delivery.
- Addition of a new protocol: this was to allow the testing of optimal infusion rates of adeno-associated viral vectors.

The following queries were raised:

- **Do you need to use heparinised saline to flush the catheters?**
The project licence holder advised this was something that they had routinely done, however he had since done a literature search to see what had been published in the comparison of using heparinised saline to saline for patency of catheters. For dogs it seemed that saline was as good as heparinised saline for maintaining patency, so he would be happy to use saline. He would double check with the anaesthetists to make sure that they were not aware of any adverse effects from using saline.
- **What monitoring would be done for any animal that had to be lone housed for 48 hours whilst the catheters were in place? Was there a plan in place if an animal became distressed?**
The project licence holder advised that the lone housing was needed to ensure that the catheters were not accidentally removed by their littermates. It was possible that the procedure could be done in pairs though in which case the puppies would be kept together. If a puppy became distressed then they would be comforted. It was agreed that this should be added to the protocol so that it could be seen that these aspects had considered.
- **When would the animal start to receive the infusion? Was it immediately after recovery from the general anaesthesia?**
The plan was to place the catheter the day before and then start the infusion the following morning, to ensure that the effects of the anaesthesia had waned as much as possible before giving the infusion as they did not want the effects of the anaesthesia to complicate the results. The detail that it would be a minimum of 12 hours after recovery from anaesthesia would be added to the licence.
- **Clarification had been requested about the very high fluid rate and the reasons for it. Did the project licence holder anticipate fluid overload issues and pressure shifts especially in young dogs?**
The high volume infusion was needed as it was difficult to manufacture viral vector at high concentration. With this volume and infusion rate they were dealing with manufacturer

protocols to the best of their ability. The 20ml/kg/hr infusion rate was already in the licence for protocol 4 (IV administration). The maximum volume of 180ml/kg was included to make it clear that there was no intention for the 20ml/kg/hr to be administered for the full 24 hour period. Problems had not been experienced previously in administering these infusion rates into the puppies.

The NVS advised that his concern related to the maximum volume and whether that could be tolerated. After discussion it was agreed that the project licence holder would seek advice on whether the proposed maximum rate of 20ml/kg/hr up to a maximum volume of 180ml/kg could be tolerated. [Secretary note: Advice has been sought and the project licence holder advised that from a heart/lung point of view this should be ok, but that one thing that should be considered is that at that age, their kidneys would have very limited concentrating capability so this overall fluid regime would cause quite a bit of diuresis. It was therefore recommended that they be closely checked for dehydration for a couple of days afterward, perhaps by tracking their body weight to see if it dropped to below pre-treatment. Wording had therefore been added to say that the dogs would be closely monitored after infusions to make sure they did not become dehydrated].

Other AWERB queries:

- **Why were the infusions being done in 4 week old puppies?**
There were two reasons: the total dose required was lower as they were puppies and so weighed less. The 2nd reason was that this was the equivalent in age to the boys that were being treated with DMD (before severe muscle changes started happening).
- **If the puppies did have to be individually housed would they be in close proximity to other puppies and be able to see them, or be in a completely separate room?**
The procedure was done in a separate room as basically they became genetically modified at that point. As a drug was being administered, under A(SP)A they were not allowed to have a companion puppy with them. One option though if there were two animals of the same age, in the same litter and suitable for treatment, it might be possible to administer the drug at the same time to both puppies so they could then keep each other company during the process. The actual infusion was a non-invasive procedure so there should not be any adverse signs, but that if there were, the animals would be separated.
- **Would the puppies be acclimatised to the procedure room before hand in order that they became familiar with it and reduce their anxiety?**
It was confirmed that at 4 weeks the puppies would not normally have been introduced to the procedure rooms but it was something they could start doing at an early stage for these puppies. Also, for the “cat” crates that would be used to keep the puppies in during the infusions, they could be introduced to those too so that they were familiar and comfortable with them.
- **Were the dogs fed during the long term infusions?**
Yes they would probably be fed every couple of hours – this would be added to the protocol.

The project licence holder was thanked for attending the meeting. He would make the suggested changes to the project licence which would then be forwarded to a sub group of AWERB to review and to confirm on behalf of AWERB whether they were happy with the changes.

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MINUTES

The minutes of the meeting held on 5th October were confirmed as an accurate record.

3 MATTERS ARISING

3.1 Item 3.1: Condition 18 training (5 October 2021 meeting)

The Home Office have advised that they would be circulating the slide set from this workshop and the updated guidance after the final training but this had not yet been received. Once this had been provided a meeting would be held to determine a practical plan for taking forward the condition 18 reporting and providing messaging to project licence holders to make them aware.

3.2 Item 3.2: Pony (05 October 2021 meeting)

The condition 18 report had been submitted to the Home Office. Receipt had been confirmed.

3.3 Item 3.3: End of PPL and mid term report templates (05 October 2021 meeting)

The amended templates had been circulated and were due to be discussed at the 9th November meeting.

3.4 Item 3.4: Keeping large animals at Camden (5 October 2021 meeting)

A check was being done to see when the next scheduled appointment with the fire brigade was as that would be an ideal opportunity to speak to them about whether the area by the stables was the most appropriate emergency access point for them.

3.5 Item 3.6: Fish (5 October 2021 meeting)

A meeting had been held involving the fish users, where squeezing of fish had been discussed. The key point was to make sure that squeezing of fish was only done at suitable time points and for suitable reasons. Over the past year or so as there had been less people around the squeezing had been done for reasons that would not typically occur. The fish needed to be bred regularly, but there were alternative ways of doing that than squeezing to reduce the risk of the fish becoming egg bound in the first place. A couple of techniques were discussed at the meeting and training would be arranged on these techniques. This would hopefully reduce the number of zebrafish that needed to be squeezed to prevent them becoming eggbound. Generally the aim was to reduce the number of fish that needed to undergo this technique. It was agreed that this action should remain as amber until the process had been reviewed and rolled out.

3.6 Item 3.6: Fish – UV lighting (5 October 2021 meeting)

The UV lighting issues had been resolved by replacing part of the kit.

3.7 Item 3.7: Establishment Licence: updating the room names (05 October 2021 meeting)

A discussion was needed with ASRU about how best to update the Establishment Licence with the required name changes to the rooms and whether it was possible to upload a site plan of the establishment with the room names set out on it to ASPeL.

It was agreed that it was important to have a site plan even if it was only internally, that set out which species could be used in which room.

A query was raised whether PIL Holders could access the Establishment Licence information that was on ASPeL. NACWOs could but there was uncertainty if PPL Holders were able to. This would be looked into.

3.8 Item 3.9: End of PPL review (5 October 2021 meeting)

The outstanding end of PPL review had still not been received but it was understood that the project licence holder was scheduled to be away for most of October and November.

The Establishment Licence Holder reported that he had agreed a sanctions approach with the Chair for those project licence holders who failed to provide timely reports. He would be sending reminder

e-mails to those individuals reminding them of their responsibilities and copying their Head of Department in.

3.9 Item 3,11: ARRIVE compliance report (05 October 2021 meeting)

The Sub Group were working on the agenda for the suggested workshop. A full update was planned for the next meeting.

3.10 Item 4: AWERB membership (5 October 2021 meeting)

A draft call was with the Chair for sign off for new internal lay panel members. A call had gone out for student members to join the Sub Committees. This call had just closed and there were a lot of applications to join AWERB.

4 [ALL ABOUT THE AWERB – “WEEK 2”](#): INDUCTION AND ENGAGEMENT

The Deputy Chair asked whether people had managed to review this? Did they have any comments to feed in? AWERB discussed what should be provided to new members.

- E1 and L course: new members should do this course as it provided an ethical background to the Act, as well as details on the Act's requirements and other related legislation.
- Induction meeting to be held with the Chair in order to go through the terms of reference
- Have a mentor on AWERB that had sat on AWERB for a while that they could go to for advice
- An information sheet to be put together detailing what the purpose of AWERB was and what looking for people to contribute

Engagement:

- How much knowledge was there of the animal work that was carried out at the College within departments, particularly those such as Estates who would be required to enter BSU areas? It should be included within inductions.
- Animal research questions should also be included as standard at interviews to make sure the applicants were comfortable that the College did animal research. This was done within some departments but it was not known how wide spread it was. The Establishment Licence Holder would liaise with HR on this.
- Ensuring there was information on AWERB available: currently summary minutes and case studies of animal research was provided on the website and intranet.
- Getting the virtual tours of BSU up and running would also increase the knowledge and awareness of other departments.
- How does AWERB engage with scientists? After scientists have attended AWERB to discuss their project licences they were sent a questionnaire to ask how they had found the experience and whether there were any areas that AWERB could improve on. So far, the feedback received had been very positive.
- How does AWERB engage with animal technicians? The NACWOs were very involved as they received the minutes and had opportunity to attend the AWERB meetings. The animal technicians were not so involved though. Before Covid they had been encouraged to attend the AWERB meetings, however during the pandemic this had not been possible due to the increased workload. It was hoped though that with the pandemic easing, that technicians might be able to attend again.

5 PROJECT LICENCE AMENDMENT

The project licence holder and his team were welcomed to the meeting. They explained the changes they were wanting to make to their project licence.

- Increasing the maximum number of animals from 6000 to 15000: this increase was required as they were wanting to develop new studies following an increase in their funding

allocation. This would allow them to investigate gene therapy in a number of ciliopathies for which they would use new mouse lines.

- Allowing the use of mice under protocol 2 to be used under protocol 3 and vice versa as they would like to trial the administration of substances via the intracranial/systemic route (protocol 2) and the retinal route (protocol 3) in either order.

AWERB had requested further information on both of these changes:

- the jump in animal numbers was quite significant and they needed to discuss the statistical justification and also general practicalities within the current RVC facility provision.
- How the flow through from protocol 2 and 3 would work. There was also concern that it might not be clear what the animals would experience moving between the two protocols.

The project licence holder and his team explained why they needed to expand the colony. A summary of the numbers of animals used so far under each protocol was provided as well as information about what the plans were for the future and how they expected they would generate the required numbers of animals. It was confirmed that all females would either be bred up to 6 months or 6 litters maximum (whichever occurred first); and that all males would only be bred up to 8 months maximum (rather than the specified 1 year in the project licence) as it had been noted that their productivity then tailed off. The proposed cage numbers were also set out.

There was discussion about the proposal of being able to have mice move between protocols 2 and 3 and how it should best be written as there was uncertainty about what the Home Office would require. Some mice would start on protocol 2 and have the some of the procedures before moving to protocol 3; whilst others would start on protocol 3 and then move to protocol 2. It was suggested that for the mandatory steps that they currently had in each protocol as optional in each other protocol instead. It would not change what happened to the mice but would make it flow better. After discussion it was agreed that the project licence should be submitted as it was for this section to see what the Home Office Inspector then advised.

It was agreed though that there should be clarification included in the project plan that there could potentially be a double route of administration and why it was required [Secretary note: it was confirmed after the meeting that there was already a sentence to that effect in the project licence but that a statement would also be added to the project plan]

The project licence holder and his team were thanked for attending the meeting. The project licence would be amended to take account of the AWERB comments that had already been provided and then recirculated for a final check.

After they had left the meeting AWERB discussed that it had been useful to hear their thought processes and justifications on the number of animals required. They had also been impressed with how the proposed amendments had been presented and how they had worked their way through them. They confirmed that subject to the requested changes, they were happy with the project licence amendment.

6 DATE OF NEXT MEETING

The date of the next AWERB meeting was confirmed as 9th November 2021.

Secretary
1 November 2021