



Minutes

Date Wednesday, 07/07/2021

Time 9:00 AM

To Committee Members

At Virtual via Microsoft Teams

Subject AWERB 3Rs Committee

In Attendance:

Minutes-

Apologies -

1. Minutes

The previous minutes were approved after a minor adjustment

2. Matters Arising

3. Retrospective Reviews

- - Prevention of chronic heart failure
- The committee discussed the following:
 - 2.1 –Totals in the columns need adding up correctly.
 - 2.9 – Answers for this section, and 2.11 and 3.10.
 - 2.10 – This states that the AKITA strain were bred in house, therefore the committee asks that reconsiders the “n/a” answer to section 2.8 concerning breeding strategies. This model could also be considered to provide a Refinement as well as a Reduction, so please add to section 3.2 and 3.7.
 - 2.13 – The committee asks that the wording “a slight overshoot” be rephrased in the light of the FOI - able nature of this document. In addition, “substantial” is no longer the correct terminology and should be replaced with “severe”, please.
The committee would also like to emphasise that if any animals are expected to experience severe severities on a protocol that the protocol remain classified as Severe, particularly considering the percentage of those experiencing severe actual severity increased year on year. Otherwise, Standard Condition 18 reporting and potential non-compliances ensue.
 - The committee felt that this content was a Refinement, and could offer a Reduction as well, so please move to sections 3.2 and 3.7.
 - 3.3 – The AWERB is keen to promote tissue sharing, and so would encourage this moving forward.
 - 3.7 – The committee would like more consideration into the answer for refinements made to the techniques or models. There was concern for example, that improving surgical ability should not be considered a refinement unless has altered or improved the procedure



itself. The celebration of increasing the team's surgical ability could be made in section 3.5 instead.

- 3.8 – The committee asks that more detail be given regarding the “electronic documentation”.
- 4.8 – The committee would like [REDACTED] to review the instructions for this section, as with the significant success of the AKITA mice as outlined in 2.10, this 3Rs achievement has very likely been disseminated.
- 5.1 – The committee asks that [REDACTED] remove the reference to rats in this section, as this licence does not involve rats.
- [REDACTED] - Induction, assessment and prevention of adhesions
- 2.1 – The committee wonders whether as no sheep were used in this licence, will sheep be included in the next one?
- 2.11 – Please detail the source/ supplier of the animals specifically.
- 3.1 – The committee would like to draw [REDACTED] attention to the work of [REDACTED] co-founder and CEO being [REDACTED] on the AWERB 3Rs committee, who has done extensive work developing a translatable-to-human mouse model of adhesions. The committees would like to know how much consideration has gone into looking at lower species for this work.
- 3.7 – The committee asks that inclusion of the [REDACTED] staff's work into handling and pre-training pigs, and any other pre terminal anaesthetic refinements made, be included here too. The same may apply to section 3.8.
- Section 4 – The committee were concerned that there was not much information put down here regarding benefits of this work considering that the work has been stated as having gone as planned, in 4.2. The committee therefore suggests that [REDACTED] re-address's the intended outputs and benefits as written in the expiring PPL in order to inspire more comments here.
- It was also noted that there were no publications listed in 4.8 - would this be because this work is for a commercial company, and if so could a brief explanation of why be included?
- [REDACTED] - Mice with transgenic immunoglobulin loci
- 2.4 – The committee would like more information please regarding the reasons as to why animals undergoing Surgical Embryo Transfer should be being found dead. If this is still on an ongoing issue please discuss with the NVS and NACWO for support.
- 2.7 – The committee takes on board comments concerning the use of the word “wastage”. The future wording of this section will be reviewed.
- 2.8 – The committee was intrigued and impressed by the “predictor” algorithm. We look forward to more detail and evidence of its reduction success in the 5-year Retrospective Review.
- 2.9 – The AWERB at the University of Cambridge is supportive of tissue and strain sharing both within the university and to the industry as a whole. Please could more explanation be given around your answers not to share? If Intellectual Property is a concern, do MTAs not protect that? Are there other ways of sharing and making use of surplus animals/ tissues that do not risk the proprietary alleles unique to [REDACTED]?



- 3.2 – The committee would like to ask whether a percentage of animal number reduction achieved could be estimated to provide some context.
- 3.7 – The committee supports and highly commends the use of analgesia and anaesthesia when performing HDTV.
- 5.2 – The committee noted the large number of SC18 reports that have been filed already during the tenure of this licence. Especially as only two animals are noted in 2.1 as having exceeded protocol severity. Please could a summary paragraph or some text-providing context be added? If these are ongoing issues, or issues that are likely to reoccur, please discuss this with and inform the NVS and NACWO.

4. Amendments

5. Project licence applications

- [REDACTED] – Discovery of novel compounds for the treatment of dementia -
Sever severity application

Intranasal (AA) only

- The committee were not convinced by the rationale provided in the amendment.
- Concern was expressed that the total volume to be given (50uL 3 times a day if less than 10 days, as per the tables), considering the nares volume of a rat (mouse would therefore be smaller) is 3uL per side, would result in inhaled into the lung or swallowed into the stomach administration, thereby not achieving the desired dosing route into the brain.
- The committee would like the details in the tables checked to ensure they are appropriate for these studies.
- Concern was expressed concerning the formulation of the drug – e.g., aqueous is readily absorbed but needs a rapid PK, whereas a more viscous preparation can lead to animal distress.
- Concern was expressed that as described the procedure would be better for the animals, and provide better drug uptake, if performed under anaesthesia.
- The committees would advise more consideration around these points be submitted and can arrange 1-2-1 personal expertise support, if required.

CNS cannulated with minipump

- The committee agrees that this procedure is industry-wide recognised, but also notes that it is technically quite challenging. Therefore, the committee would like to support where possible, good quality training, supervision, and competency assessment for this technique. Are the surgical skills already present within the team?

Behavioural tests

- The committees had no concerns with these procedures.

Tauopathy (P301S)

- The committee were impressed with the application concerning the P301S mice – this seemed thorough and well considered, and with possibly earlier end points than seen with others using this model.



- The committee advised Protocol 10 be kept as severe, but see a possibility that the HOI may consider this experience, as written, to be moderate.

Nuak1 Knockout

- The committee were very impressed with the breeding strategy and description of how these animals will be used to protect their welfare.
- [REDACTED] – Applying Regenerative Neuroimmunology to Chronic Spinal Cord Injury Research
- The committee supports the decision to split the work into multiple licences – we hope that this leads to improve and ease the management of regulated work under ASPA.
- The committee were interested to read about data mining as a replacement. The committee looks forward to hearing any follow-up on this at the end of this licence tenure.
- The committee were intrigued about how the experimental design and assessment of treatment outcomes is affected by the spontaneous recovery nature of the injury. Can more information about the challenges faced and outputs obtained be put in the Experimental Design section?
- The justification for 56 days for the duration of the study was unclear – please elaborate more in the Protocol Justification section.
- The committee would like more information on the CSF collection method as the NTS describes this as “minimally invasive”. Please could a brief description of how it is done be included in the protocol.
- The committee noted the mention of maximum number of procedures, particularly concerning the ICV injection and CSF sampling. Please could details of when these take place, and the timings between be included in the Animal Experience section.
- The committee would like to encourage the continued refinement of all endpoints for severe protocols. Please note that endpoints should be specific and not include provisos such as “unless in the opinion of”.
- The committee commends the group on a well-written licence.

6. Standard Condition 18 reports

7. 3Rs information/reports

8. Feedback from previous Retrospective Reviews*

9. Highlights of AWERB Standing meeting*

10. Highlights of January AOC meeting*

11. Any Other Business

- [REDACTED] re use of needle recommendation advice from AWRRB to [REDACTED] update. Item complete can now be removed from agenda.
- AWERB 3Rs guidance – On going



- CFA use guidance- Update, Please see circulated document.
[REDACTED] welcomed feedback. Can now go on website
- Single use of needles guidance – On going
- Hydrodynamic tail vein injection guidance – On going
- Embryo transfer Workshop – Please see circulated document
- NSET / SET – On-going
- Update on [REDACTED] PPL application – **HO refused application**

Date of next meeting: 1st September 2021

***Items for information only unless un-starred by committee member**