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Minutes

Date Wednesday, 02/09/2020

Time 08.30am

To Committee Members

At Virtual via Microsoft Teams

Subject AWERB 3Rs Committee

In Attendance:

[REDACTED]

1. Minutes

The previous minutes were approved

2. Matters Arising

3. Retrospective Reviews

The committee discussed the following:

- [REDACTED] - Understanding energy balance in health and disease
- The committee were pleased to see that usage is well within that predicted, along with very honest explanations, and that the engagement in major translational projects makes the data from these mice even more powerful.
- The committee agreed that the decreased numbers of animals due to the mite infestation is not to be considered a Reduction – as the PPLh is not gaining the same amount of data from fewer mice, in this instance. This is already covered in 2.6.
- The 3Rs committee were pleased to see suitable actions taken with regards to the SC18 reports and the error around the fasting durations – this is evidence of due diligence being undertaken. The committee recommends that the use of post-mortem examinations be part of the investigation of any subsequent unexpected adverse events.
- The 3Rs committee were very interested in how work with *Drosophila* flies have influenced the rodent work, leading to significant replacement and reductions. The committee would like to promote this and take this information forward – The committee would like to contact the PPLh for more information in due course.
- The committee were also very interested in the daily pre-testing handling and the longer period of acclimatisation enabling better results from fewer animals. There was presumably some good collaboration with the animal technicians and NACWO, and the committee would like to promote this too. A Refinement such as this, enabling better data with fewer mice, should be shared and celebrated, and be of use to others.
- The committee would like to see more information in the Replacement area about the fact that the PPLh did not need to perform novel melanocortin agonist models in mice, as human studies answered your objective goals successfully – the committee congratulated the PPLh



- The committee were very impressed with the quality of the results and the importance of the findings of the 2020 Nature paper.
- The committee would like more information on the apparent wastage, and only using male animals – Could a statement be included addressing the rationale being only using a single sex, please?
- It was widely felt that this was an honest, thorough, and well written Retrospective Review, with some very impressive 3Rs

- [REDACTED] - Tregs in lymphopaenia associated autoimmunity

- The committee recognise that there were problems with the breeding and maintaining of NSG mice. It is recognised that they can be problematic, the committee were satisfied that the PPLh is using collaborations, the PST team and the named people to help overcome this. It would be advisable to put in a statement however, outlining the approach to moving forward.
- The committee were very interested in the comment about finding NSG mice responding better to more frequent cage cleanouts. What sort of data, and in what form, is there on this? The committee would like to contact the PPLh about this in due course.
- The 3Rs committee were interested to see that the PPLh was able to create a GvHD model using the lower published dose of 200 rads. The committee is very interested in the information that is available on this please, for wider dissemination.
- It was noted that there were no publications yet associated with this PPL. Please can the PPLh mention papers or work in preparation as well as those under review.
- The committee were very sympathetic to the delays experienced in gaining MTAs (Materials Transfer Agreements). This retrospective review has resurfaced this ongoing problem to UBS.
- The committee thanked [REDACTED] for an informative Retrospective Review.

- [REDACTED] - Cell-specific chromatin profiling in mouse cortex

- The committee congratulated the PPLh on such beautiful, pioneering work. There is a solid foundation due to the in-vitro and *Drosophila* work, and we recognise this work as really being at the forefront of science. The committee are hopeful that future work will continue to be as impressive. The committee would like to promote the use of *Drosophila* to provide information for any others thinking of using them – The committee would like to contact the PPLh for more information in due course.
- The committee recognise that the first protocol could not be pursued due to personnel reasons – the committee were grateful for the explanation.
- The committee would like the inconsistency addressed. In section, 2.10 it states that some mice came from [REDACTED] yet 2.11 says 100% were from the [REDACTED] If this could be amended, please, to denote the percentage of overall animals used that came from [REDACTED]
- The committee gave thanked the PPLh for the engagement and working with the NVS and named people in respect to the two mice that died, and to refining the surgical procedures.



- Will any of the publications that are either under review or in preparation contain any 3Rs content? Will there be any 3Rs advances on the papers referenced in, e.g., 3.1?
- This was a very well written form – The committee look forward to the PPL application and the potential reductions that this work suggests!

4. Retrospective Assessments

(a) None

5. Project Licence Applications

██████████ - Mechanisms and treatment of pulmonary vascular diseases-4. (Word document to be reviewed)

- The committee recognise that the applicant's experiences of animal models and genetic diseases places them in a good place to be able to reduce animal numbers as much as possible. The numbers given are based on experiences and standard formulae and this is the same for every protocol. The committee advises tailoring and detailing the formulae more clearly, with a reference or source, so that the person undertaking the procedure can check their own understanding? The committee also think that the parameters need to be better defined, e.g., which way round the ratios are, etc. It should be written in a way so that anyone reading it would thereby know exactly what it is that they need to do.
- The committee would like some further clarification on the pulmonary artery banding procedure that is being classified as severe because of the known loss of 10% of the animals:
 - As this is due to incorrect re-inflation of the lungs after surgery – do the mice die whilst under anaesthesia or during recovery? If so, does it need classifying as a severe experience? Particularly if it is spotted quickly and the animal killed immediately.
 - Is the incorrect re-inflation of the lungs the *only* reason for post-operative death? Is this therefore operator dependent? With a more experienced surgeon, is this still as low as one can get the percentage? Is it therefore the shear nature of the model?
 - Are there other reasons/ experiences of the mice during the study that make this a severe procedure and if so this ought to be made clearer in the Animal Experience section.
- The committee were pleased to see refinements previously developed with collaborators being brought forward into this new licence.
- The committee were surprised to see the expectation of only 25% of rats on the Sugeng-hypoxia model to experience moderate. That would be fantastic if that can be achieved and demonstrated at the end of the licence in the Retrospective Review.
- The committee wondered whether or not there was a reason to down-play the achievements and role of Morphogen-IX in the future. It was felt that the benefits coming from Morphogen-IX would really sway the Harms Benefit Analysis for this licence and this work.
- The committee would like to ask whether or not ██████████ is still the most appropriate person to hold this project licence, or whether this is now the opportunity to pass on ownership of this licence to a senior member of the group?



6. Severe Severity licence reviews

7. Standard Condition 18 reports

8. 3Rs information/reports

9. Feedback from previous Retrospective Reviews*

None

10. Minutes of AOC meeting*

None

11. Minutes of AWERB Standing meeting*

None

12. Any Other Business

- The committee discussed a request received to be able to re-use needles from [REDACTED]. The committee felt it was best to invite [REDACTED] so she could present her plans in detail so the committee are better informed to be able to make a decision on whether to allow the re-use of needles.
- It was agreed that [REDACTED] would send an email to the committee regarding membership and acceptance of meeting invites
- The committee discussed how to engage better with researchers and technicians about 3Rs.
- Reducing the length of RRs was discussed to allow time for other discussions in meetings
- Advertising the UBS website more was discussed – How & to who

Date of next meeting: 3rd March 2021

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