MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 23 June 2022

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 26 May 2022 were approved subject to a correction of the typographical error where the wording should have been "alveolar macrophages".

2. Applications for New Project Licences

2.1. [redacted], Immune Regulation of Health & Disease in Mucosal Barrier Tissues

Considered: A completed AWERB form, PPL application, and minutes from Local Management Committee Meeting.

Interviewed: [redacted]

Discussed:
- The application is not clear on if there is sufficient money to cover the work.

- The licence is well written and clear.
- The committee were impressed with the presentation and wonder if it can be used as an example of what people should be doing. Licence applicants are given the time for the presentation and told to do 5 slides addressing 5 specific points. The difference between presentations may be due to style when talking rather than the contents of the PowerPoint presentation.

Revisions:

- Please include in the licence that repeated dosing will be done using alternate flanks.
- Page 13 – Funding. Please reword the section to explain the funding available to support the studies. Replace with current research grant funding i.e. total grant awards etc.
- Page 22 - On the one hand you say that sex has been well documented to significantly impact on immune responses. But on the other you say you do not expect sex to be a key determining factor in experimental outcomes. Please can you clarify this as the two statements seem to contradict each other.
- Page 40 – Please can you expand on what 'severe or prolonged' is in relation to the endpoints. Are these determined on a scale?
- Page 48 - what is the rationale for steps 1 and 2 on this protocol? Could these be combined as mandatory on more than one occasion?
- Page 84 – Are Methotrexate and Doxorubicin likely to have effects on the animals?
- Page 87 - There are multiple mentions of the EDA - is it possible to include an example diagram using this tool.
- Page 89 – Step 3 – Please correct the typos as follows: DREADD ligands will be **given** ad lib in drinking water or via the diet wherever possible, or in some cases **may** be provided via an oral or injectable route in a maximum volume of 200ul per dose will a maximal dosing regimen of daily dosing for two weeks.
- Page 102/103 - A fasting period of 12h is stated in protocol 6 - step 4 but in adverse effects 18h is mentioned. Please clarify which is correct.
- Page 109 - Bacterial Infection – Please correct the typo as follows: 'While the majority of animals used in this protocol are expected to tolerate infection well and **exhibit** signs of mild severity…'
- Page 115 - For protocol 6 there appears to be a mistake (under animal experience) as to which steps are likely to be performed - "Step 1, Step 1 or this Step....." is mentioned? This also happens on page 140.
- Page 126 - Where in the licence this statement is made it should be altered to " In rare cases (<10%) Germ free or monocolonised/minimally colonized mice can develop spontaneous caecal torsion, which can manifest as rapid weight loss and morbidity that requires euthanasia of the animal".
- Page 126 - Microbial colonization of Germ Free mice – the sentence should end '**weight** loss'.
- Page 126 (pdf version). Where in the license this statement "In rare cases (<10%) Germ Free mice can develop spontaneous cecal torsion, which can manifest as rapid weight loss and morbidity that requires euthanasia of the animal" is made it should be altered to " In rare cases (<10%)Germ free *or monocolonised/minimally colonized* mice can develop spontaneous caecal torsion, which can manifest as rapid weight loss and morbidity that requires euthanasia of the animal"

- Page 127 - In step 2 Diptheria is spelled incorrectly.
- Page 132 - How will you monitor for, control, and limit any of these adverse effects? – Please correct the typo as follows: 'Mice will be provided with mash or hydrogel to ensure hydration and nutrition in the **event** of weight loss…'
- A number of comments were made regarding your Non-Technical Summary which are listed below. Please update your NTS based on the comments and send it to the following lay members for their review [redacted])
    - Page 2 and 3 - commensal bacteria is mentioned on p.2; a good clear definition of what this means for the lay reader is on p.3 ('or "good bacteria" that reside in our guts'). I wonder if this explanation could be moved to appear on first use of commensal to help the non-expert lay reader.
    - Page 3 - The second half of the "Why is it important" paragraph gets a little circular in how it refers to diseases. Please can you look at rewording this.
    - Page 4 - I would edit the 'who will benefit' section slightly to add how critically important this basic research is rather than allowing the line "it is unlikely any immediate clinical benefit will be seen within the duration of this Project" to be a take home message.
    - Page 5 - I feel that in the "what will be done to the animals" section of the NTS it's good to describe what procedures are being used such as intraperitonal injection, oral gavage, blood sampling, transient anaesthesia with isofluorane etc.
    - Page 6 - What are the expected impacts – second paragraph, last sentence. Up **to** a period of weeks.
    - Page 6 - Your style of presenting information is very clear for the lay reader, so the paragraph beginning "In many cases" stands out as introducing a number of technical terms which aren't explained - e.g. immunomodulatory, bacterial modulation. Please include explanations for these.
    - Page 6 – Please reword the sentence 'it is expected some prolonged adverse effects of mild to moderate severity will be experienced, with durations exceeding 12 hours and up a period of weeks' as per the discussion in the meeting where you explained that the model is over a period of weeks but the adverse effects are a number of days within that model.
    - Page 7 - 3rd paragraph beginning "There are currently" includes the phrase "a highly tractable model" . Please include an explanation for this or consider rewording for a lay reader.
    - Page 7 - Why were they not suitable? the second sentence seems to get lost at "in which immune cells". Please consider rewording this sentence.
    - Page 8 – Reduction. How have you estimated the numbers of animals you will use? Please seek advice from the Named Persons if previous experience is sufficient as a basis for estimating the number of animals.

There is also a lot of detail here for a lay reader so please seek advice on if this all needs to be included.

- Page 8 - Reduction. What steps did you take during the experimental design phase to reduce the number of animals being used in this project? If you have previous findings to support the two-fold increase/decrease please can you include reference to these in the licence.

Outcome: The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

2.2. [redacted], Pathology & Treatment of Orphan Diseases

Considered: A completed AWERB form, PPL application, and minutes from Local Management Committee Meeting

Interviewed: [redacted]

Discussed:

- The revised draft submitted to AWERB following the pre-AWERB meeting has not been checked as [redacted] was on leave when it was submitted.
- This is a large and complex licence.
- The group discussed moving animals between protocols to ensure they stay within the appropriate severity band. The committee were advised that this had been discussed at the pre-AWERB meeting and the applicant advised by the BSF that breeding should be listed as 'moderate', but the applicant wanted to keep the animals on a 'mild' protocol until they display a 'moderate' phenotype.
- The licence contains mention of sheep however this was not raised with the statistician.

Revisions:

- There are a number of abbreviations used but not all are described on the first use. Please look to explain these at the first usage and reduce the number of abbreviations where possible.
- For the different mouse strains specifically highlighted please use the correct names e.g. not Okabe mice or Pep 3 mice. Perhaps at least a more genetic version if not the full nomenclature.
- Please check consistency of humane endpoints throughout the licence. The committee appreciate it is a big licence but please ensure the appropriate end points match the protocols throughout.
- Reword where it says "bodyweight of 20% or greater…. In humane endpoints. Needs to be much more specific/accurate and get agreement with NACWOs etc.
- Please seek guidance from the Named Persons if reference to accepted guidelines for injections etc, somewhere be included in the document.
- As discussed in the meeting, the number of procedures that an animal can have is not clear in the licence as it is currently written. Please work with the Named Persons to ensure it is clear what procedures can be done on the same animal and which options you would not combine.
- Page 17 - Please change PolyIC to Poly I:C here and elsewhere in the application.
- Page 26 – The use of "homos" and "hets" is an abbreviation which is not common English and should be avoided.

- Page 29 – please clarify what you mean by 'replacing' over-vigorous males. Do you mean they are euthanised? Is over-vigorous defined objectively?
- Page 31 – please clarify what is meant by 'Depending on the lines being crossed'
- Page 41 – Protocol 3 and Protocol 4 - Rats are said to be used in these protocols but there is no indication in which Steps they will be used. Please can you include this information. The use in both Protocols takes the total number of rats to be used to 300 which is greater than the number shown on Cat A form. Please clarify and update as necessary.
- Page 47 - For this protocol 3 it states in adverse effects that occasionally food withdrawal for up to 16 hours is required. Please seek advice from the Named Person if this needs to be stated in the protocol as a step and associated adverse effects listed. This is also the case for protocols 4-7.
- Page 47 – Please can you clarify if 10 minutes for the water maze test is a standard length of time.
- Page 52 – Please clarify why the mice require more samples of their ear tissue to be taken? This will also potentially happen in the next step. Or is the subsequent step included in error? This applies to the subsequent protocols.
- Page 64 – Step 1 – 'either' is followed by 'and/or'. Is this correct?
- Page 68 - As written, mice could receive conditioned cells via all of the routes. Is this intended or should it be written or, not and/or?
- Page 88 - The multiple routes of administration require some work to constrain what you are requesting authority for.
- Page 97 – Please include an explanation for the use of a diet lacking is soy products.
- Page 112 and following: Should "Immunogeneic" actually be "immunogenic"?
- Page 135 – Protocol 7 - There is no indication in Protocol 7 that MPS111B are used. However on page 140 and thereafter reference is made to them. Is this just a pasting error or should the MPS series be specified on page 137?
- Page 142 – please clarify how frequent 'regular scoring is'.
- Page 148 – please check the amount for the hydrodynamic injection as 2.5mls seems excessive.
- Page 166 – Please include a reference for the sheep grimace score if one is available.
- Page 166 – please clarify how frequent the 'frequent observations' are that will be undertaken following surgery.
- Page 168 – please clarify how CSF sampling is acquired.
- Page 172 – the example used for statistical power is one for mice, however this protocol is for sheep. Please update.
- Page 215 – please can you explain why you re-genotype? Could this not be collected post-mortem? Do you often find mistakes in your genotyping? Typically most groups do not re-genotype live animals as standard.
- A number of comments were made regarding your Non-Technical Summary which are listed below. Please update your NTS based on the comments and send it to the following lay members for their review [redacted]

[redacted])

- The NTS as it stands is very difficult to read for a lay member.
- Page 2 – please include an explanation of what orphan diseases are in the section 'What's the aim of this project?'.
- Page 4 – please reword 'How have you estimated the numbers of animals you will use?' as it is slightly unclear at the moment.
- Page 4 - I think the "why is it important" paragraph gives too much detail for the NTS, without helping the lay reader understand to some degree the diseases referred to, and hence the relevance of the proposed research. It wasn't until I was reading the first paragraph on page 8 and came across ""these progressive childhood metabolic diseases" that I understood what sort of conditions were being researched. I think you are assuming too much from the reader of what is intended as the Non-Technical Summary.
- Page 4 - For the lay reader "transplantation" suggests organ transplants. Please clarify in the application.
- Page 4 - First paragraph: referring to "diseases such as MPSII and MPSIIIA" doesn't help the lay reader. Please use alternative names for the diseases where possible or use a general explanation.
- Page 5 – please reword 'never more than 20%' to make it clear that weight loss will not exceed a humane endpoint of not more than 20%.
- Page 5 - This line could be misconstrued: some models are very slow, so we use immumomodulators to make them more severe and rapid." The word 'severe' might be confused with a statutory severity level so I'd remove "severe and"
- Page 6 - The "severities" paragraph only makes sense if the reader has the various protocols available to them which isn't the case, since it is only the NTS which is posted on the public website. Please reword this.
- Page 7 – please expand on the section 'How have you estimated the numbers of animals you will use?'. Previous experience should be expanded on to include specific results seen from previous work, while keeping the section brief and for a lay reader.
- Page 9 - Perhaps add in refinement a few lines on the use of analgesia, post-operative care, aseptic technique etc. (rather than in 'what will be done to the animals')?

Outcome: The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

3. Retrospective Assessments of Project Licences requiring full committee review

3.1. [redacted], [redacted] Modulation of inflammation in the GI tract.

Considered: A completed Retrospective Assessment form.

Interviewed: [redacted]

Discussed:

- You completed 51 studies for 39 different Sponsors during the lifetime of the Project Licence.
- You will follow up with the Sponsors regarding publication of the data.
- The number of animals reported as 'severe' is reassuringly low despite Protocol 1 having a severity banding of 'severe'.

Revisions:

- Questions 13 - The numbers requested and used are identical. The committee believe that the number of animals requested for use should actually be higher than those used. Please can you update the form accordingly and return this to me.

Outcome: AWERB endorse submission of the Retrospective Assessment subject to the revisions above being made and reviewed and approved by [redacted] on behalf of AWERB.

4. Report on licences processed from 06/05/2022 to 02/06/2022

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], The Role & Regulation of Reactive Oxygen Species in Development & Regeneration.

5. Update on applications outstanding from previous meetings and upcoming Project Licence applications

5.1. The committee were provided with a document showing the status of applications considered previously and those pencilled in for future meetings. A number of those listed have now been granted.

6. NACWO and Directors report

6.1. No comments made on the report submitted.

7. NVS report

7.1. The report showed that lots of good practice is happening.

7.2. A report on the review/audit of the anaesthesia equipment will be provided in a future meeting.

8. Standard Conditions 18s and non-compliances

8.1. The committee were provided with a table of reports submitted to ASRU along with the reports for each incident. ASRU stated no further action for the following two reports:

[redacted]

9. Any other business

9.1. Guidance Use of Standard Genetically Altered (GA) Animal Protocols

The standard wording for protocols for GA mouse and zebrafish breeding have been updated. They now include more refined approaches and are formatted according to the new style ASPeL project licence application.

9.2. Home Office Inspection

No feedback has been provided as yet from ASRU following the inspection.

9.3. Be Open Animal Research

The Deputy Chair expressed thanks to MA for this work on the Be Open About Animal Research Day (#BOARD22).
Three case studies were produced along with a video:
https://www.manchester.ac.uk/research/environment/governance/ethics/animals/outcomes/replacement-reduction-refinement/fruit-flies/
https://www.manchester.ac.uk/research/environment/governance/ethics/animals/outcomes/replacement-reduction-refinement/breast-cancer/
https://www.manchester.ac.uk/research/environment/governance/ethics/animals/outcomes/replacement-reduction-refinement/cystic-fibrosis/
https://www.youtube.com/watch?v=8-KDtoXtdts&t=2s&ab_channel=TheUniversityofManchester

---

The next meeting will be on 21 July 2022 at 10am-12.30pm.

Dates of meetings for the 2021/2022 academic year are:
21 July 2022

Dates of meetings for the 2022/2023 academic year are:
22 September 2022
20 October 2022
17 November 2022
15 December 2022
26 January 2023
23 February 2023
23 March 2023
27 April 2023
25 May 2023
22 June 2023
20 July 2023
August break