MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 14 November 2019

Present: [redacted]

Apologies: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 19 September 2019 were approved.

2. **Applications for New Project Licences**

2.1. [redacted], Melanoma Formation, Immune Responses & Evaluating Novel Therapeutic Approaches & Agents

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

Interviewed: [redacted]

Discussed:

- For protocol 3, the application states that n=2 which the committee queried regarding the tolerability studies. The applicant explained that 2 mice will be used in the first instance but then a higher number of animals would be used to obtain statistics. Please can you clarify this in your application.
- For Protocol 2, the Committee asked for clarification about the number of animals that would be at the top end of Moderate or potentially enter a Severe categorisation. The Committee recommend that you discuss this Protocol with the Home Office

Inspector for advice on which severity banding this protocol should enter. Consideration should be taken over whether this systemic model is done as a separate small protocol with a Severe banding.

- Some members of the Committee were concerned about the lack of experience of the applicant has in working with mice. The Committee were reassured that there are members of staff named on the application that are experienced at working with mice. The committee recognise that [redacted] is an experienced researcher with Zebrafish and ask that he takes the same level of oversight in this licence as the BSF staff indicate he does in his work with Zebrafish.
- The applicant used a number of phrases during the discussion which concerned the committee such as “pin down”. The Committee would ask the applicant to consider his use of language when discussing working with mice so that it is clear that the mice will be handled appropriately.
- The Committee raised the number of imaging sessions that the mice would have, and suggest some alternative wording be used to clarify how many sessions of imaging an animal would undergo. Please contact [redacted] for advice on the wording in your application.
- The Committee ask that the number of animals listed on the AWERB form and Home Office application be checked to ensure that they match up.
- The Committee discussed the problems with measuring 40% food and water consumption is the animals are group housed. The committee suggest that you weigh the animals at least twice weekly. Please can you include this in the application if you are going to implement this.

Revisions:

- The committee asked for information on the reasons your studies will be carried out in females only. The Committee still had concerns about the reasons you stated and would like you to address this in your response to them and in the application itself.
- Please ensure that in your application you confirm/highlight that needles will only be used once when sampling or administrating substances to mice.
- When you mention body condition scores please can you check that you have the symbol the correct way round. Should this read 'body condition score >2' i.e. when a body condition score is greater than 2? It is written as body condition score <2 - I think the symbol is the wrong way round?
- There were a number of points not raised during the committee regarding your lay summary. [redacted] would be willing to work with you to improve the contents. The points include:
    - CAR (please explain in parenthesis)
    - Would prefer: By the end of the project we HOPE TO have validated several novel potential therapeutic targets for treating advanced melanoma (which may be of relevance to other malignancies). We also AIM TO generate insight into resistance to immune check point inhibitors, which may well prove to be actionable (i.e. targetable by a drug). Further, we AIM TO generate and evaluate the safety and efficacy of a

novel CAR to a melanoma surface protein. Our findings will be disseminated at scientific meetings and in publications and our reagents licensed where appropriate for commercial development.

- Please clarify what you mean by “This may happen only years after the project has been completed”.
- You may wish to change the wording to: To reduce any suffering of tumour bearing animals, animals will be HUMANELY KILLED as soon as tumour formation is sufficient to yield satisfactory data and always before animals become moribund, manifest severe pain or lose significant weight (which is closely followed).
- The committee wold suggest: Local experience reveals that this has most frequently been associated with weight loss (DELETE due to cytokine release syndromes) in less than 20% of all experimental animals and has been managed through close observation and the provision of hydropacks and mash (EXPLAIN WHAT hydropacks and mash are).
- The question to the question "Which non-animal alternatives did you consider for use in this project?" seemed to be answered with adjunct non-animal techniques that were being used; which is fine I think though the sense I had of the question was more about which non-animal techniques were considered and ruled out (with explanation in answer to the subsequent question).
- Also, the sentence "Co-culture systems can begin to address interactions between different cell types but not the entire spectrum" was difficult to understand; should it be part of the next question's answer or is it saying the non-animal techniques in use only go so far? Some clarification here would be helpful perhaps.

- There appear to be many abbreviations without indication of what most of them mean.

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], Mechanistic Insight Into/Assessment of Novel Therapies for/Preeclampsia & Fetal Growth Restriction

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

Interviewed: [redacted]

Discussed:

- [redacted] had been provided with a reference by [redacted] regarding data in the literature to suggest that, in order to see the largest difference in glucose tolerance in mice fed a high fat diet, a 6 hour fast, followed by oral dosing of glucose is most effective. The committee discussed with the application if they had considered these changes for the glucose tolerance test protocol.

- The Committee asked the applicants if considered making provision for adding a second hit in this in Protocol 4 in the event that no programming effects are observed?

Revisions:

- Members of the committee felt that the Protocol Summary is too detailed and should be more brief, concise and succinct. If you would like advice on revising this you can contact our lay members, [redacted] for advice.
- Specific comments on the Protocol Summary were:
    - is it possible to explain briefly what "preeclampsia" is in some way - if only through its symptoms? I presume fetal growth restriction is as it sounds - diminished growth of child. On p.4 of the AWERB form there is a nice sentence which does more to explain these conditions - " such as preeclampsia, characterised by maternal high blood pressure and deterioration in kidney function, and fetal growth restriction, a baby that does not grow as well as it should." - perhaps this sentence could come earlier so the reader has a sense from the start.
    - P8 of AWERB form, sentence that contains " significant adverse effects (i.e. that do not cause significant ....." - the '(' needs removing or a closing ")" is required
    - Please explain what EDA is.
- There are a few typos which could be altered including:
    - Page 92 penultimate line delete “which”
    - Page 10, first line under “What are the humane endpoints...” “deterioration” not “deteriorated”
    - Page 104 first line in “How will experiments and.....” “advance” not “advanced”.
- The occurrence of adverse effects is frequently given with indicative numbers as to how often this is likely but on page 56 of the licence (and elsewhere) there is a statement that very occasionally haematoma or bruising may occur without any numerical indication of frequency. Please can you include these.

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

2.3. [redacted], Breeding & Maintenance of Genetically Altered Zebrafis

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

Interviewed: [redacted]

Discussed:

- The application is for a service licence for the breeding and maintenance of genetically altered Zebrafish.
- The committee asked if the applicant has an effective plan for outreach, publicity and advocacy to encourage local researchers to consider adopting Zebrafish models? The BSF staff explained that at pre-AWERB meetings they always ask researchers looking to work with other species if Zebrafish could be used instead.

Revisions:

- There are a few typographical errors which needs correcting:
  - P3 of the PPL experimental not experimental
  - P9 of the PPL, in section 'How do you assure quality' - use 'show' not 'should'
- The committee suggest in the Replacement section - use 'in vitro' instead of 'in test tubes'.
- Could you more concisely explain what 'pre-protected' and 'protected' means for zebra fish in lay language; this would help for lay reader.
- In the section, Who or what will benefit from these outputs, and how?, it may be worth including if there is any benefit from the animals being on one breeding licence directly for the animals. Centralization seems to imply potential standardization of welfare practice and would presumably make it easier to sustain and improve care and welfare practice efficiently.
- In the Reduction section, would careful management to align production with need ensure minimal animals are produced and maintained? If so, please include this in the application.

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. Applications for Amendments to Project Licences requiring full committee review

3.1. [redacted], [redacted], The Role of Inflammation in Cerebrovascular Disease.

Considered: A Home Office amendment summary sheet.

Interviewed: [redacted]

Discussed:

- The amendment sought a change in the severity category from moderate to severe in Protocol 3.
- Protocol 3 allows ICH in up to 1000 mice/rats (minus the naïve, control, and shams) with ~8% (up to 80) entering the current moderate band. If the protocol was changed to Severe then the committee had concerns with allowing the provision for 1000 animals to enter a Severe banding. The Committee discussed that the applicant should consider how many animals they do require based on their Home Office returns and amend the number in this Protocol accordingly.
- The Committee welcomed the applicants being proactive in raising the need for a change in severity banding based on the researchers work on this licence so far.
- The committee suggest that the applicants make allowances in the licence for mid-procedure mortality.

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

The amendment was given approval.

4. Report on licences processed from 30/08/2019 to 24/10/2019

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted] MK2, as a Regulator of Inflammation in Alzheimer's Disease (Transfer to UoM).
[redacted] Anti-Cancer Therapy Validation
[redacted], Designing Therapeutic & Diagnostic Nanotechnologies for Medicine
[redacted], Pregnancy Complications: Targeted Interventions
[redacted], Type 2 Immunity in Infection & Tissue Homeostasis

4.2. Amendments to Project Licence [redacted]; Generation, Breeding and Maintenance of Genetically Altered Rodents

[redacted], Generation of an IL-1α D106A Mouse Line Using CRISPR
[redacted], Generation of a Haptoglobin Flox Mouse Line Using CRISPR

5. Update on applications outstanding from previous meetings

5.1. [redacted], Defining Critical Regulatory Pathways Controlling Local & Distal Immune Responses During Health & Inflammation of Barrier Surfaces.

To report: Home Office has fed back on the submitted draft and [redacted] needs to make changes and submit these back to the executive committee.

5.2. [redacted], Mechanisms of Diabetes-Associated Heart Disease

To report: [redacted] will be submitting a revised application for consideration at a future AWERB meeting.

5.3. [redacted], [redacted], The Aetiology of Diabetic Neuropathy.

To report: Revisions still to be submitted.

6. NC3Rs Regional Programme Manager update

An Experiment Design workshop was run a few weeks ago and a lot of people attended. Technicians are going to be invited to a slightly altered workshop in the future.

7. Any other business

7.1. AWERB away day

The away day took place on Friday 11 October 2019 and the Secretary will circulate the meeting notes and papers.

7.2. Euthanasia in fish

The BSF requested support from AWERB to move from the current method of confirming death in fish to freezing the euthanised fish as the confirmatory method. This change would require an amendment to the establishment licence. Members of AWERB present agreed that the new method was appropriate.

The next meeting will be on Thursday 23 January 2020 at 10am-12pm, in [redacted].
