The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 19 September 2019

Present: [redacted]

Apologies: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 4 July 2019 were approved.

2. Applications for New Project Licences

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

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

Interviewed: [redacted]

Discussed:

- Some aspects of the application require rewrite in order to improve the application prior to submission to the Home Office. The Committee have obtained permission from an experienced licence holder for their application to be shared with [redacted] so that improvements can be made in terms of scientific writing style and grammar.
- The committee were concerned about the mortality rate of 30%. They would like to see this reduced.

- The committee queried 5mg/kg LPS in protocol 3 and advise that this is reconsidered to be lower based on other studies taking place at the University of Manchester.
- STZ-induced diabetes model can be a difficult model to work with, particularly in mice. The applicant may see some mice with little change in blood glucose concentration, and some with very high concentrations. The applicant was advised to use a blood glucose concentration cut-off point i.e. if it reaches a certain level those mice will be removed from the study.
- The committee discussed with the applicant the "30 studies" in protocol 2. Please revise in the application if 30 studies are being carried out. This would mean that to 1920x0.3=576 mice to enter the "substantial severity" band. If 30 studies are being carried out, please consider whether some of these studies could be avoided in milder protocols (even if that would require more animals overall), reserving protocol 2 for the smallest number of truly pivotal studies.
- Approval from the BSF staff needs to be sought before the work can progress to the severe protocol. The model should be established first given that it has not been used at the University of Manchester previously.

Revisions:

- Please consider whether the power calculation is too severe (e.g. why do you need to detect an interaction between genotype and intervention of as small as 5.5% - why not 10% or 20%?)
- Please clarify if you have taken into account possible drop-outs in the STZ group, i.e. mice with very high or low blood glucose concentrations that cannot undergo the next step of the procedure.
- The NTS should be revised to address the following points:
    - "Few thousands of animals" is not appropriate. The expected numbers should be stated.
    - [redacted], a lay member on the committee can assist with revision of the NTS.
    - We advise that you change "necessary" (under Reduction) to "appropriate".
    - Reduction - The applicant should mention use of longitudinal studies / imaging modalities in this section.
    - Refinement - There is a lot of repetitive information in this section which doesn't really address the questions asked. Please revise.
- Please revise the sentence regarding ARRIVE guidelines. ARRIVE are reporting guidelines - not guidelines per se on how to conduct the research in the first place therefore the committee advise that you remove this from the Reduction section.
- On page 30 (under Termination of the Experiment) the two statements are incompatible. Please revise.
- Please clarify in Protocol 2 the diet for the control group - this be grain-based chow or a control purified diet? This can impact measures of glucose tolerance.
- In the project plan, part 4, it is stated that "The animals will be sacrificed once different cardiac function is observed between the treated and untreated mice, or impaired cardiac function or frequent arrhythmia occurs in any experimental group". What happens if there

is no effect of the manipulation (pharmacological or gene delivered activator), how long to you keep going for? Please include a guide to the time-frame you will use to monitor the animal for an effect before you end the experiment.

- Protocols 2 and 3. In Step 1 - Induction of diabetes, you say that you will "induce diabetes with modified diet or injection of chemical inducer (STZ) on wild type mice". Are you using a transgenic mice in this model too?
- In Protocol 2 you say that "Any animal ...showing signs of dehydration (such as loss of skin elasticity, tenting of skin for more than 2 seconds when gently pinched)...will be immediately killed by S1..." Is there any scope to treat the dehydration at an early stage to avoid loss of experimental animals?
- That some aspects of the application require rewrite in order to improve the application prior to submission to the Home Office. The applicant should discuss this with [redacted] and use the attached licence from [redacted] to facilitate the necessary improvements that need to be made in terms of scientific writing style and grammar. [redacted] is NOT to be approached for help.

Outcome: The revised application will need to be reviewed by the full AWERB committee given the number of revisions/clarifications outlined above. The applicant will need to return to a committee meeting to discuss how the application has been altered.

2.2. [redacted], The Aetiology of Diabetic Neuropathy

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

Interviewed: [redacted]

Discussed:

- Both rats and mice are being used under the project licence. The Committee discussed with the applicant why two species were being used.
- The committee asked for some additional information on the Cystometry procedure.
- The committee queried the percentage of animals undergoing both STZ and an altered diet.

Revisions:

- Please include some more information in the licence about why both rats and mice are being used.
- Please include some more information about the cytometry procedure.
- Please speak with the NVS in the BSF about the number of animals that are going to undergo which procedure (STZ and an altered diet) and include clarification of the numbers of animals, including controls, in the application.
- In liaison with the NVS in the BSF, please include some further information on the justification for using a unilateral nerve crush injury to the sciatic nerve.

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], New Therapeutic Approaches for Inflammatory Joint Disorders.

Considered: A Home Office amendment summary sheet.

Interviewed: [redacted]

Revisions: None

Outcome: The amendment was given approval.

3.2. [redacted], PKCα & Vascular Calcification in Kidney Dysfunction.

Considered: A Home Office amendment summary sheet.

Interviewed: [redacted]

Discussed:

- The amendment to change a protocol from moderate to severe is being sought in response to a number of unexpected deaths of animals. 4 out of 63 animals died unexpectedly.
- The unexpected deaths were sporadic and did not occur at a specific time point in the licence. The researchers have never observed the deaths on similar previous licences; the use of a new mouse strain may the reason behind the deaths.
- The procedure for surgery will be changed such that surgeries will be carried out in the afternoon/evening so that there are more staff within the BSF in the morning during the risk period.
- There is a traffic light system for monitoring mice after surgery.

Revisions: None

Outcome: The amendment was given approval.

4. Report on licences processed from 20/06/2019 to 29/08/2019

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], Zebrafish: Development, Physiology & Disease Modelling.
[redacted], Neural Basis of Tactile Behaviour.
[redacted], The Role of Circadian Clocks in Immunity.
[redacted], A Study on Treatment & Penetrance of Inherited Cardiac Conditions.
[redacted], Regulation of Glomerular Barrier Function in Health and Disease.
[redacted], Circadian Regulation of Processes Underlying Chronic Inflammation.
[redacted] (prev [redacted]), Brainstem Circuits Controlling Gut-Brain Communication (Transfer to UoM).

[redacted] (prev [redacted]), Radiolabelled Molecules for Cancer Imaging & Therapy (Transfer to UoM).
[redacted], Cardiac Conduction System in Health & Disease (Change of PPL Holder).

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

[redacted], Generation of a C57BL/6J.Timd4^{Em1Uman} Mouse Model Using CRISPR.
[redacted], Generation of a C57BL/6J.Timd4^{Em2Uman} Mouse Model Using CRISPR.
[redacted], Generation of C57BL/6J.RyR$^{SNAP/AgBP2Uman}$ (RyRAg SNAP) Mouse Line Using CRISPR.
[redacted], Generation of a TOMATO-SOX7 Mouse Line.
[redacted], Generation of a VENUS-RUNX1b Mouse Line.
[redacted], Generation of a Tor1a^{rescue} Mouse Line Using CRISPR.

4.3. Applications for secondary availability for new or current project licences

[redacted], The Interactions of Innate & Adaptive Immunity ([redacted]).

5. Update on applications outstanding from previous meetings

5.1. [redacted], Fish Physiology in an Era of Climate Change.

To report: Revisions have not yet been submitted by the applicant.

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

To report: The Home Office required major revisions to the project licence which is currently with the applicant.

6. NW region AWERB hub

- The NW region hub was hosted by [redacted].
- [redacted] attended.
- The next hub meeting will take place in February/March and be hosted by [redacted].

7. NC3Rs Regional Programme Manager update

7.1. NC3Rs workshop on experimental design

On the 1st of November the NC3Rs are running a workshop on experimental design. This will include discussion about best practice in experimental design, e.g., randomisation, etc., in addition to a demonstration of the Experimental Design Assistant. [redacted] will circulate information on the event to the PIL distribution list.

7.2. ARRIVE guidelines

The ARRIVE guidelines are being revised and [redacted] will be speaking about this at the away day.

7.3. Home Office thematic review about single use of needles

The Home Office have recently done a thematic review on the single use of needles and a poster is being produced.

8. Any other business

8.1. AWERB processes

- The notes from the meeting held on 10th June 2019 between [redacted] were shared with members for their information and input. No issues were raised regarding the content of the document which covered managing project licence renewals, meeting schedule, the processing of amendments and Named Persons comments on the AWERB form.
- A draft communication was provided covering the notification of current PPL holders of the process and timeline for submitting applications for renewal of their PPLs. A discussion took place regarding the sanctions for applicants that did not meet the expectations set out in the communication. The issue will be discussed further at the away day.

8.2. AWERB membership

- [redacted] has resigned due to a new position at the University.
- [redacted] will start on the committee as of 1st January 2020.
- [redacted] has accepted the offer to extend her term by another 3 years.
- [redacted] will join the committee on 14th November as a lay member.
- Some thought needs to be given to future lay membership given that for a number of lay members their term of serving on AWERB is due to end in the next couple of years.

8.3. AWERB away day

The away day is taking place on Friday 11th October, from 12-5pm.

8.4. Process for reporting on licences processed

Currently the NVS verbally summarises the minor amendments that have been processed. At the next meeting the Chair will ask if AWERB members have any questions regarding the list of licences processed since the last meeting. If there are no questions then the NVS will not verbally go through the amendments.

8.5. Amendment documentation

For amendments considered by the full AWERB committee the Secretary will ensure that a full PPL is circulated along with the amendment summary sheet to ensure that members have additional information on which to consider the amendment request.

8.6. Paperwork at future meetings

The Home Office have released a new system for applying for a project licence. The applications will appear different in the new form. The questions are more concise but there may be an increase in the number of pages per application.

The next meeting will be on 14 November 2019 at 10am-12pm,
in [redacted].

Dates of meetings for the 2019/2020 academic year are:

17th January 2019, [redacted]

14th March 2019, [redacted]

16th May 2019, [redacted]

4th July 2019, [redacted]