MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 25 May 2023

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 27 April 2023 were approved.

2. Retrospective Assessments of Project Licences requiring full committee review

2.1. [redacted], Determining important regulatory pathways that control immune responses to infection

Considered: A completed Retrospective Assessment form.

Interviewed: [redacted]

Discussed with applicant:

- The committee queried if oral gavage was necessary for administration of the infection in Protocol 3 given there had been an incident in which a mouse was found to be showing signs of distress and suffering with the most likely caused by a misplaced gavage during dosing. The researcher explained that while oral gavage can be replaced by administration of for example analgesics in water, this would not be appropriate for the administration of a bacterium as

part of an experimental technique. AWERB were assured that oral gavage was appropriate in this context and that the researcher who had conducted the procedure in this instance was appropriately trained in the technique.

- The researcher explained that the mice found dead in cages did not appear to be strain related. The committee discussed that mice can spontaneously die and the number of deaths in this way on the licence was not abnormal and the percentage of animals dying not due to experiment/protocol reasons was actually very low in this case.
- The licence holder explained that major refinements are hard to implement in their work due to the nature of the infections being investigated, but they are always trying to refine the procedures to reduce severity levels.

Outcome: AWERB support submission of this Retrospective Assessment to the Home Office

3. Applications for New Project Licences

3.1. [redacted], Identifying the Critical Downstream Targets of ROS During Tissue Repair & Regeneration

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

Interviewed: [redacted]

Committee discussion:

- The statistician explained that he has only recently seen this project licence and provided the applicant with feedback. The statistician explained that his advice had not changed the numbers or methodology of the application. It was noted that the statistician's review and sign-off should take place prior to any future applications coming to committee.

Discussed with applicant:

- The possibility of the work being translated into clinic was discussed.
- Sham surgery was discussed with the researcher.

Revisions: It was explained to the applicant that the committee had provided comments to the Secretariat prior to the meeting and while some would be discussed in the meeting, the list below includes all the comments whether they were raised in the meeting or not.

- Following a discussion in the meeting, please contact ASRU for regulatory advice on if tail clipping with anaesthesia should be moderate or mild severity.
- There are a couple of typographical errors in the licence and it would benefit from these being corrected, e.g. page 7 "This makes zebrafish particularly useful ***for*** investigating the genetic, cellular and molecular mechanisms of tissue repair" and ***advice***, rather than "advise" on a number of occasions.
- Title - From a lay perspective the title "Identifying the critical downstream targets of ROS during tissue repair and regeneration" is not comprehensible in any meaningful way; is it possible to convey the purpose of the project in less technical language?

- Protocol 4 - Please remove the reference to “sham surgery of the ventricle to include thoracic incision, opening of pericardium, without injuring the heart” and other references to sham surgery as discussed in the meeting.
- As discussed in the meeting, please emphasise that the use of cell lines and *in vitro* testing is used to test the toxicity of previously untested compounds before you move into using zebrafish.
- Protocol 3 and 4 steps 1, 3 and 4 - How will you monitor for, control, and limit any of these adverse effects? Please can this be expanded on in Protocol 3, steps 1, 3 and 4. How will you monitor? Are you using score sheets? What is the frequency of monitoring if you are using novel compounds? In terms of limiting adverse effects - how are you doing this? Are you using analgesia for example?
- Protocol 3 & 4 steps 3 and 4 - Can you please explain 'aim to be' when talking about drug dosing for the tank or for injections. Will you use known physiological doses and only change this if there are no effects from the dosing?
- Protocol 4 - You only mention starving for anaesthesia in this protocol but not in protocol 3 or anywhere else you mention possibly using anaesthesia. Is there a reason for this?
- Page 14 - In the long paragraph starting "Here we aim to extend…." there are multiple examples of abbreviations which are not explained the first instance they are used. Please can you check that the licence explains abbreviations the first time they appear.
- Page 35 - In the paragraph starting with "Fish are anaesthetised…." Please check with the BSF if the specific anaesthetic should be stated.
- 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]
    - Overall, this is a clear NTS, it might require more work to explain actually happens to the zebrafish other than the fin and heart damage.
    - It may be beneficial if some of the longer sentences are broken up to make the NTS easier to read for the lay audience.
    - Please can a number of terms in the NTS be expressed in less technical language or concisely explained for lay readers, e.g. "critical downstream targets", "reactive oxygen species", "transiently modulating" and " downstream protein mediators".
    - Page 2 - The "Why is it important to undertake this work?" is a little over detailed – and would benefit from answering the question clearly at the start, followed by a longer explanation if needed. The importance seems to be in working out the role of H202 in regeneration with the long-term goal being that this could then inform future human therapeutic interventions to promote regeneration? Presumably this would help with wound healing?

- Page 5 – Please include a description of what data/results you are obtaining and how, and what happens to these zebrafish in the collection of such data.
- Page 4 - There are two sections labelled as "Short Term benefit". Is this correct?
- Page 8 - "we are constantly looking to further refine them to minimise the numbers needed and also the potential harms." Should this be "we are constantly looking to further refine them to minimise potential harms" as later in paragraph you address reduction?
- Page 8 – Please conclude a little more on the methods you might need to use to minimise pain, suffering and distress. Perhaps you can explain how you immobilise the fish for instance, obtain gametes, or use imaging probes? Some explanation of how and when the fish are given analgesia and anaesthesia would be helpful.
- Page 8 – Please explained why the repeat injections are needed.
- Please include an explanation of how the heart injury might physically impact on the animal (if it does) in the two months before it heals.

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

4. Report on licences processed from 12/04/2023 to 10/05/2023

The following amendments were approved by the executive committee and provided to AWERB for information.

4.1. Amendments to Project Licences

[redacted], Factors Regulating the Skin Immune System in Health & Disease

[redacted], Genetic & External Influences on Regulation of the Immune System

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.

6. Directors and NACWO report

6.1. No comments were made on the report submitted.

6.2. The Director of the BSF also reported that:
The technique of cross-fostering has proven successful in eradicating Helicobacter spp. from two lines. The success was confirmed by two consecutive rounds of negative test

samples. Lastly, a new Contract Research Organization (CRO) specializing in telemetry studies will be integrated into the BSF in the upcoming months.
The [redacted] will be visiting the University of Manchester (UoM) in September or October to discover possible avenues for collaboration.
A visit to the Biological Sciences Facility (BSF) is also planned by our PELh, where he will be conducting a tour and participating in an Establishment Assurance Group (EAG) meeting in October, with the exact date to be determined.

7. Analgesia guidance

7.1. A further discussion took place regarding the use of drugs being used off-label and if AWERB should have a statement about this. AWERB was of the opinion that they support the use of drugs being used off-label in the BSF under NVS guidance and backing, but noted that the use of a blanket statement may lead to difficulties should a decision have to be made regarding the use of a generic or branded version of a drug.

8. RSPCA/AWERB hub maximising the effectiveness of AWERB

8.1. The Chair commented on what an interesting meeting it had been. The slides from the meeting have already been circulated by the AWERB Secretary.

8.2. The Director stated that the Director of AAALAC had been very impressed with the event and positive about the Chair's level of engagement.

9. Any other business

9.1. AWERB 'away day' 30 May 2023

The Secretary of AWERB reminded people of the AWERB 'away day' taking place on 30 May and encouraged as many people as possible to attend.

The next meeting will be on 22 June 2023 at 10am-12.30pm.

Dates of meetings for the 2022/2023 academic year are:
22 June 2023
20 July 2023
August break

Dates of meetings for the 2023/2024 academic year are:
21 September 2023
19 October 2023
16 November 2023
14 December 2023
25 January 2024
22 February 2024
21 March 2024
25 April 2024
23 May 2024

20 June 2024
25 July 2024
August break