ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 22 February 2024

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 25 January 2024 were approved.

2. **Applications for New Project Licences**

2.1. [redacted], Understanding Visual Processing in Freely Moving Animals

Considered: A completed AWERB form and PPL application

Interviewed: [redacted]

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.

- A discussion took place between committee members regarding the justification for this licence. It was felt that further details of potential clinical applications would be beneficial.

- Page 15 - the suggestion to potentially replace some of the animal studies detailed in protocol 5 with human studies could be framed to more explicitly convey that there is a prospect but currently (or within the tenure of this PPL) there would be no substantial basis to proceed with replacing animal experiments.
- Page 27 - Why is there a termination step for the non-invasive observation protocol? Is it simply to provide a comparator? Is there not data you could use off the shelf for this?
- Page 28 - the mention of sham surgeries appears to be redundant, considering that no surgeries are anticipated for protocol 2. Please remove reference to sham surgeries if this is the case.
- Page 34 - Please clarify how/why "Damage to camera mount and/or light source" is as an adverse effect. The question is asking about adverse effects to the animals.
- Page 36 - It seems there could be a discrepancy with the number of recording in protocol 3. On page 36, Step 4 suggests up to 5 recordings, whereas the "Animal Experience Section" on page 37 mentions that recording may be repeated up to 10 times. Please can you double check this.
- 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 an excellent NTS - very clear and remarkably concise.
    - Page 2 - Great concise and clear description of aim. You could drop 'overarching' for the lay reader just to simplify.
    - Page 3 - to help the lay reader follow meaning could your consider revising "physically constrained (3R's Refinement)" to something like "physically constrained (thereby advancing 3R's Refinement)"?
    - Page 5 - not a major issue but "We are interested in how the visual system functions and how it controls behaviours" repeats the same sentence used prior (top of p.4) . Not necessary really although overall the NTS is succinct.

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], Role of Microglia & Blood-Brain Barrier in Dementia

Considered: A completed AWERB form and PPL application

Interviewed: [redacted]

Committee discussion:
- This application came to pre-AWERB meetings quite late therefore there are more points that need addressing in the application than usual. The committee noted that there were no specific welfare or ethical concerns.

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.

- Please ensure that a thorough check of all answers is carried out, as some answers appear to be incorrect, e.g. Page 16 – “Does your project mainly involve translational or veterinary clinical applications?”, you have answered ‘yes’ but the committee think this should be ‘no’.
- Page 31 - Please clarify the animal numbers as in Protocol 1 it states 2000 but in Protocol 2 it states 2500 and also that animals will be obtained from protocol 1. Will the other 500 be obtained from somewhere else or do numbers need to change?
- Page 33 - Out of interest for the adverse effects - how will you monitor hearing loss and sight problems - will the latter effect any of the behavioural tests used?
- Page 34 - Will you really give treatments for 3 days only? - at least this appears to be what is written?
- Page 35 - In adverse effects you mention patients - do you mean to say mice? This is also the case in Page 53.
- Page 35 - In the humane endpoints section, immobility is stated as a humane endpoint and results in culling the animal, whilst in the above section it says this is seen in less than 20% of animals (which could still be quite a lot). Maybe it would be better to state "prolonged (>30 min) immobility" as the humane endpoint instead?
- Page 38 - For imaging frequency - It is not clear what 'repeat measurements will only last for 6 weeks' means (and this is possibly the same for Page 40) and the other protocols. Please clarify.
- Page 41 - for monitoring of adverse effects it mentions chronic high-fat diet-treated mice having hypertension but where in this protocol are you high-fat feeding?
- Page 43 - There are some discrepancies in weight loss endpoints - in one section it states 15% weight loss compared to preceding month, and in another simply "weight loss 20%". Please can you ensure the percentage is consistent.
- Page 47 - You mention NLRP3 inflammasome but is this a focus of your studies?
- Page 49 - If only 25% animals are expected to undergo recovery surgery (the other 25% surgical are non-recovery), then how did you get 50% expected to be moderate? This is the same in Protocol 2.
- Page 49 - Step 1 - would it be sensible to add wording to allow administration of normal chow for controls as step 1 is mandatory. Please seek guidance from the Named Persons.
- Page 52 - How do you include lean controls as cage mates? Wouldn't they just eat the HFD? Please clarify this.
- Page 67 and 91 – The statement about NLRP3 inflammasome and IL-1 is not relevant for this project therefore please remove.
- Page 70 - Step 3 - would it be sensible to add wording to allow no surgery for controls as this step is mandatory. Please seek guidance from the Named Persons.
- Page 74 - You have tamoxifen injection for transgene induction in this protocol – Please can you check if this is needed for your other protocols.

- Page 76 - For monitoring - you mention 'related to cerebral ischaemia' but is this what you are doing here? You also mention MCAo but you are using the common carotid. The text also mentions stroke - so this section needs to be reworded to align with the vascular dementia model you are using rather than a model of stroke.
- Page 88 - For experimental groups you mention inflammatory inducer e.g. LPS here but no mention of this in injection of 'substances' or anywhere in this protocol and it does not seem clear from background you will be causing inflammation/infection. Is the mention of LPS included in error?
- 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 - "The aim is to study of the roles of immune cell and blood-brain barrier dysfunction in different stages of dementia" – please remove of.
    - Page 3 - "Dementia is an age-related brain disorder in which the patient has an impaired ability to remember, think, or make decisions that interferes with doing everyday activities." This reads a little odd and may benefit from breaking it up into two sentences OR altering it to read something like "Dementia is an age-related brain disorder where the patient has an impaired ability to remember, think, or make decisions, which interferes with everyday activities."
    - Page 3 - microglia - is it essential to specify? If so, can it be explained in lay terms? You could maybe just remove "specifically microglia" here for the lay reader NTS here as the next paragraph introduces them as a type of immune cell.
    - Page 4 – It may be helpful in terms of the short term benefit to explain why options such as the UK Biobank cannot provide answers to your questions about the relationship between metabolic illness and dementia in humans.
    - Page 4 - "The project has received funding from the Alzheimer's Association US to investigate the impact of amyloid antibody treatment using this unique mouse mode" – considering deleting this as it is not required information for the NTS.
    - Page 5 – Please consider changing the wording to be more specific, e.g. "mice will become heavy".
    - Page 5 - "Here's why" is a bit of an odd way to present it. Perhaps reword to "Mice are used as animal models in aging studies because:"
    - Page 6 - "BBB functions" - is there a non-technical way to express this? Also pathogenesis - is there a simpler lay term such as 'development of disease'? Or can a meaning be provided?

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. Report on licences processed from 10/01/2024 to 08/02/2024

The following amendments were approved by the executive committee.

3.1. Amendments to Project Licences

[redacted], The Long Term Effects of Developmental Hypoxia on Cardiac Function
[redacted], Understanding & Targeting the Inflammatory Response
[redacted], Genetic & External Influences on Regulation of the Immune System
[redacted], Understanding Vision & Developing Therapies for Blindness

3.2. Amendments to [redacted], Breeding and Maintenance of Genetically Altered Rodents

[redacted], Creation of GIPR-LoxTB Mouse Line Using CRISPR
Creation of IL-13-2A-eGFP Mouse Line Using CRISPR
Creation of ip43 Mouse Line Using CRISPR
Creation of HS3ST2 iCre Mouse Line Using CRISPR

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

4.1. The committee were provided with a document showing the status of applications considered previously and those pencilled in for future meetings.

5. Director and NACWO report

5.1. No comments were made on the report.

6. NVS report

6.1. No comments were made on the reports.

7. Any other business

7.1. Lay member review of NTSs

Clarification was requested on if lay members who receive the updated NTSs from applicants are expected to approve the NTS or being sent them for information. The Chair would like the lay members to approve the revised NTS.

7.2. Lay members on AWERB

More lay members need to be recruited to the committee. The Chair will look at how this can happen given the sensitivity of the committee. A discussion also took place on how to recruit to ensure more diversity on the committee.

7.3. Teams

A member of the committee raised the issue that it is distracting when Teams alerts all participants in the meeting when someone is in the lobby. It was also evident that the researcher seen first was also distracted by the notification that the second researcher had entered the lobby. It does not appear to be possible to disable this function. It was noted to also be a security issue as anyone in the meeting appears to be able to allow entry to people in the lobby. Reverting meetings to Zoom will happen until the functionality in Teams allows the meeting to be hold securely and without disruption.

The next meeting will be on 21 March 2024 at 10am-12.30pm.

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

Dates of meetings for the 2024/2025 academic year are:
19 September 2024
17 October 2024
14 November 2024
12 December 2024
30 January 2025
27 February 2025
27 March 2025
24 April 2025
29 May 2025
26 June 2025
31 July 2025
August break

Dates of meetings for the 2025/2026 academic year are:
25 September 2025
23 October 2025
20 November 2025
18 December 2025