

**ANIMAL WELFARE AND ETHICAL REVIEW BODY**

**Minutes of the meeting held on 15 April 2021**

Present:

[REDACTED]

Apologies:

[REDACTED]

In attendance:

[REDACTED]

**1. Minutes**

*Agreed:* That the minutes of the meeting held on 4 March 2021 were approved.

*Noted:* The Chair welcomed [REDACTED] and thanked [REDACTED] for doing a fantastic job as Acting Director over the past few months.

**2. Applications for New Project Licences**

**2.1. [REDACTED], Immunopathology of Experimental Blood-Stage Malaria.**

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

*Interviewed:* [REDACTED]

*Discussed:*

- AWERB were informed that an additional meeting had taken place between the applicant and BSF Named Persons after the pre-AWERB meeting.

- The applicant has had a lot of contact with the Home Office Inspectors about the severe protocols and the majority of changes requested had been incorporated into the application.
- The question had been asked if it was usual to ask the HOI about unexpected phenotypes and the NVS stated that the wording in the application was standard.
- The applicant was asked to what degree the research would be damaged if permission was denied by AWERB to support the application in its current format with a large number of animals being requested to enter the severe banding. The applicant explained that the disease progresses so quickly that in order to investigate what happens clinically the animals would have to develop cerebral malaria.
- The use of anaesthesia was discussed and the support given to animals during recovery.
- The use of analgesia was discussed. Clinically analgesia is not given so the applicants mimic the treatment as much as possible in order to translate their work.
- The committee noted the high level of experience that the applicant possess and the care that his group take with the animals.

*Revisions:*

- The use of different scales for ECM and other forms of malaria is potentially confusing. It might help if there were a single (agreed) scale to be used
- Please can you give a bit more detail on the behaviour tests on page 106/159
- Page 50 and 69. Please can you check with the BSF staff if 25% weight loss for chimeras be allowed.
- Page 73 – Please include details of how body temperature will be monitored. This should be included at all points when body temperature is mentioned.
- Page 29 – Please remove tail tipping from step 2
- Page 36 – Please remove tail tipping from step 2
- Page 37 – Please clarify why might mice need to be maintained until 15 months of age, particularly if they might develop GI inflammation from 5-6 weeks of age. The protocol later states mice of age 6-12 weeks are needed.
- Page 73 - Will steps 4 and 5 of Protocol 6 be performed on the same animals i.e. cranial window + splenectomy/lymphatic ligation? If so, at the same time or what will the gap be?
- Page 86 - Is it possible to provide an example power calculation for this model e.g. for your most commonly used strain, what number of mice are needed to observe a significant effect of treatment?
- Page 98 - Protocol 7 - will animals be subject to both a cranial window and lymphatic ligation? What will the gap between these procedures be?
- Protocol 5 Step 2 - 10 injections in total may be given, is there a minimum amount of time between injections?
- Protocol 6 - Monitoring the disease progression is clearly crucial. Can disease stage/score be as accurately monitored during the day and night? Are the checks during the night time carried out in red light or

under normal lighting conditions? Can you provide your thoughts on effect of light at night?

- Protocol 9 Step 5 - Mice will be infected with either live parasite; attenuated parasite; parasite extracts. Are the latter two more refined? If so, is it necessary to use live parasite here?
- 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

- Page 2 - 'Immunopathology' and 'blood-stage malaria' in the "What's the aim" paragraph are not helpful in the NTS, which is aimed at a public readership
- Page 3 - as above - technical terms need explaining.
- Page 4 - The "Typically" paragraph is mostly clear - but "memory immune cells" needs explaining, and "immunomodulatory" would also benefit from being 'unpacked'
- Page 11 - "Briefly summarise the current state" paragraph includes information about re-infection, repeated exposure, etc. that might usefully be included (in 'NTS wording') in the NTS, because it explains the context for the work in a clear manner.
- Page 4 of 159. Project Harms - Typically what will be done to the animals
- There might be more information with respect to the 'Injections and surgical procedures', such as 'removal of the spleen' (splenectomy), the cranial window for imaging of the brain (a simple description), 'ligation of the brain draining lymphatic system', and the careful control of the injections.
- The term "Immunomodulatory treatments" is repeated 3 times in the last 2 sentences. Could I suggest 2 replacement sentences? Multiple treatments to modulate the immune system in a single animal will be avoided when possible. Cumulative effects of adjustments to these treatments will be minimised (to allow recovery of the animals).
- Page 5 – Reduction - There is one sentence of 5 lines. This would benefit by being made succinct.
- Page 4 - Is it possible to add more precise humane endpoints for severe suffering? Maybe something like: Severe suffering will typically be for less than 4 h and not more than 12 h
- Page 4 - I don't get too much of a sense of what the animals feel for example : what the irradiation or surgery does to them or that they induce experimental cerebral malaria in the animals. As there are 5 severe protocols then it's quite important this is explained in a bit more detail
- NTS - what will be done to the animals – please can you add a line explaining that the animals will generally not receive more than 10 injections and no more than 4 injections per animal over a week? Also maybe say injections will be administered into the spinal canal and brain and cranial windows performed?

- NTS Refinement section – It may be helpful to add: Multiple treatments in a single animal will be avoided, when possible with a maximum of two separate approaches applied in any animal.
- The word "significant" is used a little liberally (e.g. four times on page 3 of 159) - which is fine though you may want to substitute alternative terms or delete some uses to avoid repetition which erodes the power of the word.
- immunomodulatory is quite a technical term - is it necessary? Perhaps define/clarify or delete? (for the lay reader)
- Might it appropriate to indicate proportion of mice that will experience non-cerebral malaria and proportion that will? I wasn't quite sure what proportion of mice may be used in such a way that mild, moderate or potentially severe suffering was the expectation but had the sense very few would be potentially exposed to severe?

*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], Brain Immune Responses Driving Behavioural Symptoms Associated With Mild Traumatic Brain Injury (mTBI) & Repeated mTBI (rmTBI).**

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

*Interviewed:* [REDACTED]

- Discussed:*
- The need for pilot work was discussed.
  - The recovery rate after the trauma was discussed. The applicant hopes to have 100% recovery rate after the trauma.
  - The model was discussed and how it may relate to real-world scenarios. The model requires a loss of consciousness whereas heading a ball during a career in football would be a different type of brain trauma.
  - The model will be replicated as per the applicants work at previous institutions. Once the work is underway an amendment could be submitted to reduce the time between injuries.

- Revisions:*
- Can the title be re-thought? As a lay reader, this tells me little that I can understand as to the purpose of the research. If the title could be rethought so as to express research aims in lay language this would be very helpful, perhaps something as simple as "Investigating how brain immune responses drive behavioural symptoms associated with mild and repeated traumatic brain injury?" this moves the title from a statement to giving more of a sense of doing. This is a minor adjustment but important as the title is the first thing we encounter and it anchors the reader. Ideally, the reader should be anchored by understanding not mild confusion. Please explain EDA the first time it is mentioned (page 7/33)
  - On page 25/33 tests are specified but without any details. Please can you provide details of the tests.
  - On page 27 does not extraction of the brain to search for immune cells need to be mentioned.

- Under Group Size (page 29/33) figures are given without units. These need to be added.
- Please can you check the whole application for grammar. There are places where singular verbs are used where they should be plural and vice versa.
- Page 18 – please explain what an electromagnetic impactor is.
- Page 24 - details on how body temperature will be monitored is not supplied. Please include this.
- Is it correct that there is no breeding protocol on this application.
- Page 9 - Typo: lead should be led.
- 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

- Page 5 - probably necessary to explain "sham" (which is done in the Technical Details section, but not in the NTS), and certainly necessary to explain "cisterna magna"
- It is anticipated that the refinement of more precise and reproducible impacts will be confirmed and therefore implemented. Please consider stating this in the 'What will be done to the animals' section.
- Page 5 of 33 - Typo -2 instances of misspelling of anaesthetic, instead of anesthetic
- Page 5 of 33 - There is something not quite right in this sentence "Animals will experience stress or transient discomfort due restraint for injection of substances or inhalation of gaseous anesthetics (100% incidence)" to my reading, should due restrain be during restraint?
- As it is presented, I am reading that 100% of mice are expected to experience moderate (substance injection) and mild (behavioural tests). If this is incorrect, could the proportions be expressed?

*Outcome:* The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB and **reporting on pilot work to the Local Management Committee within the BSF.**

### 3. Report on licences processed from 19/02/2021 to 25/03/2021

The following amendments were approved by the executive committee.

#### 3.1. Amendments to Project Licences

[REDACTED], Circadian Regulation of Processes Underlying Chronic Inflammation

[REDACTED], Evaluation of Cognitive Function in Animal Models  
[REDACTED], MK2 as a Regulator of Inflammation in Alzheimer's Disease

[REDACTED], Understanding Vision & Developing Therapies for Blindness

[REDACTED], Cell Therapy for Diseases of Striated Muscle

**3.2. Amendments to Project Licence [REDACTED]; Generation, Breeding and Maintenance of Genetically Altered Rodents**

[REDACTED], Generation of Chil3/Chil4 KO Mouse Line Using CRISPR

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

4.1. [REDACTED] licence has been submitted to the HOI. Comments have been received back and are being incorporated into the licence.

4.2. [REDACTED] licence has been submitted.

4.3. [REDACTED] has been advised that she will need to move to another meeting as deadlines have not been met for the drafting of the licence and the next meeting slot available is February 2022. The breeding animals would need to be moved onto another licence and Cathy has been advised to speak with [REDACTED] about this. No animals would be culled as a result of AWERB not reviewing the licence.

**5. NACWO report**

5.1. A second incident of animals being without water was reported. It appears that the pouch was incorrectly attached or dislodged and this wasn't picked up during routine checks. The animals were found in poor condition and one animal was culled straight away. A further two animals did not improve sufficiently and had to be culled the following day. The incident has been reported to the Home Office.

5.2. The Deputy Director talked about the strains that the BSF staff have been under during the past year and that other establishments have also reported mental health needs of technicians and staff. The new Director is looking at staffing levels as part of her review and will come back to AWERB if anything is required from them. The Chair will speak with the Director of the BSF and Academic Director of the BSF to decide if any action is needed from AWERB at the present time.

**6. NVS report**

6.1. The NVS report was circulated with the meeting papers with updates highlighted.

**7. Standard Conditions 18s**

7.1. A report of the Standard Conditions reported to the Home Office was circulated with the meeting papers.

**8. 3Rs AWERB subgroup report**

8.1. The first meeting was held on 17 March 2021 and the minutes were circulated with the meeting papers. The aims and objectives were discussed and the process of moving the mid-term reviews and retrospective reviews from the main AWERB meeting to the subgroup.

## **9. NC3Rs Regional Programme Manager update**

- 9.1. The funding round for a PhD studentship is available. A webinar was recorded about tips for submitting a good studentship application. A 3 or 4 year option is now available, whereas previously only a 3 year studentship was available.
- 9.2. Tech3Rs: A newsletter for animal technicians. The latest version is now available: <https://nc3rs.org.uk/tech3rs>
- 9.3. 10 years of CRACKing IT. 10 years ago NC3Rs year launched the CRACK IT Challenges open innovation funding competition – a new and unique approach to driving disruptive innovation in the 3Rs. The website contains highlights from the past 10 years: <https://nc3rs.org.uk/news/10-years-cracking-it>

## **10. Any other business**

- 10.1. The agenda for the extra AWERB meeting to discuss matters other than licence applications was circulated with the meeting papers.
- 10.2. Animal rights demonstrations are planned for 24th May and 6th June.

---

**The next meeting will be on 27 May 2021 at 10am-12pm,  
Via Zoom.**

---

### **Dates of meetings for the 2020/2021 academic year are:**

8 July 2021  
19 August 2021  
30 September 2021