MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 21 January 2021

Present: [redacted]

In attendance: [redacted]

Apologies: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 18 November 2020 were approved.

2. Applications for New Project Licences

2.1. [redacted] Use of Genetically Modified Biological Assemblies to Generate Improved Vaccines

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

Interviewed: [redacted]

Discussed: The committee discussed with the applicant:

- The strategy for the use of both sexes of animals. The applicant explained that this will be dependent on the planned future work for each disease, for example the manifestation of Gonorrhoea is dependent therefore any challenge experiments performed in the future would only use female mice, therefore the vaccine work for Gonorrhoea being carried out under this licence would also be in female mice.

- The lay summary would benefit from some rewording and clarifications.
- The humane end points need updating. The NVS will provide input to the applicant on this.
- The number of animals were discussed. Inclusion of additional animals will be required to enable the pilot work to be carried out.
- The use of only adult animals was raised. The applicant stated that this was so that the work was in line with other studies.
- The applicant was advised to include pilot work regarding the use of adjuvants.

Revisions:

- The number of animals you require should be increased to 700 to allow you to carry out the pilot experiments outlined in the application.
- The use of adjuvants needs to be clarified, specifically when you would use them. If you are going to run pilot experiments with adjuvants then this should be stated in the application.
- As discussed in the pre-AWERB meeting, the justification section on IP needs to be expanded on.
- As per the email from the NVS, please include "animals will be culled if they lose 15% of their pre vaccination bodyweight" alongside the humane end points you already have in for Protocol 1, Step 1.
- Step 1 in the Protocol doesn't have an anaesthetic code
- Page 18 of 28 – Please explain as you did in the meeting about the use of both sexes. Please make it clear that each agent won't be tested in both males and females but will be on one sex depending on the plans for future studies.
- Under Training (page 10 of 28) please include the training you have done, not just say it needs updating.
- Under the scientific background (page 11 of 28), the 9th line does not read properly (where it says ....serious infectious some serious infectious diseases).
- Some of the terms could do with further explanation (e.g Th1, Th2, and Th17 on page 13 of 28)
- 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]
    - Replacement - What non animal alternatives - Line 3 - A definition of the 'dendritic cell' would be useful for the lay reader.
    - I think there needs to be a bit more explanation in terms of aims: might this technology speed up the trials process? Or is it just about efficacy? Can this technology, when proven, be described as the basis for an 'all purpose' vaccine? Does the application for each pathogen need to be tweaked individually and if so, would that require a trial in its own right? Are there any infections for which it is inapplicable?

- Should the line: "The first generation of Covid19 vaccines are likely to limitations of efficacy, cost and stability" be revised?
- Can you explain in lay terms why it would not be appropriate to include animals of both sexes in all experiments?
- I felt the section on stress and monitoring is relevant to the NTS- probably the refinement section. (Stress will be minimised through the application of correct animal handling methods; all new or inexperienced licence holders will be initially supervised by BSF staff to ensure that they are competent in the procedure. Only once it is clear that the licence holder is able to carry out the procedure competently, and with minimal stress to the animal, will they be allowed to work without supervision. All animals will be monitored after vaccination for reaction at the site of injection 2 and 24 hours after inoculation. In addition, animals will also be monitored in the 24 hour period after inoculation for signs of distress and altered behaviour (eg hunched posture, reduced activity levels, altered social interaction).
- Would say humanely killed rather than just killed
- As a lay reader, I found it quite hard to imagine how the project was going to produce new vaccines as described in the NTS under 'aim'. Is the activity to genetically modify scaffold proteins? Is it possible to explain (a.) what a scaffold protein is (b.) what you will do to it or how it be used - I get the sense you can build a 'vaccine' on these scaffolds?
- I wasn't sure:
    - "The impact could be wide-ranging but will be after the conclusion of the project: vaccine development is generally a slow process and it typically takes many years for a new product to reach the market. It is important to note, however, that vaccines have saved the lives of millions of people and animals worldwide. We urgently need new approaches to address those diseases which, for a variety of reasons, have been resistant to vaccine development up to this point. It is only through further research and innovation that we will be able to overcome these challenges."
    - was all that necessary; it reads more as a defence than an explanation as to how we will benefit. Once validated, will the new technique make possible new vaccines, or a new way to develop vaccines, which is faster and/or applicable to diseases that have hitherto resisted existing vaccine development approaches? If so, could this be said clearly?

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 before proceeding to the full experiments.

3. Mid-term and retrospective reviews requiring licence holder attendance at the meeting

3.1. [redacted]**, Evaluation of cognitive function in animal models.**

Considered: A completed mid-term review form.

Interviewed: [redacted]

Discussed:
- The licence holder is now [redacted] after [redacted] retirement.
- The committee discussed with the applicants the four animals that had been recorded as having a Severe rating. The committee were reassured that steps had been taken to reduce the likelihood of issues with oral dosing happening again, and noted that this is a very rare occurrence.
- The committee raised the issues about publishing when working with pharmacological companies.
- The committee found the work extremely interesting, particularly the playpen work.
- The applicant explained that for animals receiving up to ten drugs, they can never be 100% certain that there is no carry over effect from one drug to another, however the drugs are given acutely to reduce this possibility.

Outcome: The study was given approval for continued work.

4. Applications for Amendments to Project Licences requiring full committee review

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

Considered: A Home Office amendment summary sheet.

Interviewed: [redacted]

Discussed:
- The amendment is to allow electrophysiology to measure peri-infract depolarisation.
- Pilot studies will be carried out and numbers calculated for larger experiments based on the pilot data.
- The committee discussed with the researchers if there is an interaction between anaesthesia and depolarisation. The researchers explained that some anaesthetics do block depolarisation therefore the type of anaesthetic used will minimise this interaction.
- The committee asked about how the depolarisation would be treated without treating the infarct. The researchers explained that the effect of NMDA antagonists can be separated temporally to those of the depolarisation.
- The researchers stated that the long-term aim would be to carry out the work non-invasively.

Outcome: The amendment was given approval.

5. Report on licences processed from 29/10/2020 to 31/12/2020

The following amendments were approved by the executive committee.

5.1. Amendments to Project Licences

[redacted], Pathophysiology of Heart Failure
[redacted], Assessing Novel Treatments for Endometriosis
[redacted], Regulation of Glomerular Barrier Function in Health & Disease
[redacted], Evaluation of Cognitive Function in Animal Models
[redacted], Development & Validation of Animal Models for Neurodevelopmental Disorders
[redacted], Generation, Breeding & Maintenance of Genetically Altered Rodents
[redacted], Mechanistic Insight Into/Assessment of Novel Therapies for/Preeclampsia & Fetal Growth Restriction
[redacted], Type 2 Immunity in Infection & Maintenance of Tissue Health
[redacted], Circadian Regulation of Pulmonary Immunity
[redacted], The Role & Regulation of Reactive Oxygen Species in Development & Regeneration

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

[redacted], Generation of Muc2-iCre Mouse Line Using CRISPR
[redacted], Generation of β4GalT7 Flox/Flox Mouse Line Using CRISPR
[redacted], Generation of C57BL/6J-Mettl16tm1UMAN Mouse Line Using CRISPR

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

6.1. It was reported that a few applicants are not hitting deadlines and the NVS stated that the pipeline was not working. The Chair stated that we have a process in place which the researchers are made aware of including reminders sent from the BSF about deadlines, but it is ultimately the researchers responsibility to meet the deadlines so that the workload of AWERB and the Named Persons in the BSF can be managed.

6.2. There are two new members of the University who are planning on submitting Project Licence applications. These new members would not have received any information about the expected lead in times for being considered at an AWERB meeting.

6.3. The meeting in April 2021 will be set aside for discussion about AWERB processes and other non-licence matters.

7. NACWO report

7.1. The BSF is running at full capacity with all staff working full time and not on split shifts. The researchers also appear to be back to usual.

7.2. Staff are being tested for Covid-19 via the lateral flow testing which is available to staff working on campus. No test has come back positive.

7.3. The Acting Director of the BSF is meeting with the NC3Rs Director to discuss the funding for the post of the NC3Rs Regional Programme Manager. AWERB support the funding for this post and would like to thank [redacted] for all her contributions to AWERB and the 3Rs at the university.

7.4. The Chair of AWERB thanked the Acting Director of the BSF for all his work during the pandemic and asked that AWERB's thanks be passed onto the staff at the BSF.

8. NVS report

8.1. A document was provided by the NVS to cover his updates since the last AWERB meeting

9. Standard Conditions 18s

9.1. AWERB note that there are a larger amount of SC18s than usual. The NVS explained that this covered a longer period than usual, and that the submission of SC18s was a sign that the welfare of animals is being taken seriously and any adverse events or instances of severity limits being exceed being reported to the Home Office as per the requirements.

9.2. The NVS explained that one SC18 was being investigated as a non-compliance. The NVS will provide an update, in confidence, at a future AWERB meeting once the investigation was complete.

10. NC3Rs Regional Programme Manager update

10.1. There is a workshop on 16 February focussing on how the NC3Rs are working with funders regarding what they will be looking at in their applications.

10.2. A webinar on rat tickling is taking place the week commencing 25 January 2021.

10.3. A 3Rs symposium will take place online given the constraints surrounding social distancing. [redacted] plans to have two 2 hour session on one day either in April or May.

11. Any other business

11.1. Update on the set-up of the 3Rs subgroup

[redacted] and [redacted] have agreed to join the 3Rs subgroup as Named Persons representation. Two NACWOs and a senior technician are also joining. Uptake by researchers has been minimal but this subgroup requires academics as representation. The academics on AWERB are urged to speak with their groups about the subgroup.

11.2. Research Compliance Committee (RCC) reporting to AWERB

At the March 2020 AWERB meeting it was agreed that the Research Compliance Committee (RCC) report completed by the Director of the BSF on a quarterly basis would be submitted to the preceding AWERB meeting.

RCC took place on 14 April 2020, 15 July 2020 and 29 October 2020 however AWERB have not seen these reports.

In the future, the RCC report will come to the following AWERB meeting. This will be a standing item on the agenda.

The next meeting will be on Thursday 4 March 2021 at 10am-12pm,
Via Zoom.

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

8 October 2020
Wednesday 18 November 2020
21 Jan 2021
4 March 2021
15 April 2021
27 May 2021
8 July 2021
19 August 2021 - no licences to be seen this meeting. AWERB processes meeting.
30 September 2021