MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 8 July 2021

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 27 May 2021 were approved.

2. **Actions from extra AWERB meeting held 26 May 2021**

An update on the actions arising from the extra AWERB meeting were given.
All actions are complete.

3. **Applications for New Project Licences**

3.1. [redacted], Modelling gene therapy for congenital bladder dysfunction.

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

Interviewed: [redacted]

Discussed:

- The applicant is currently completing the PIL C course after which the training section can be updated in the Home Office system.
- The technique to reduce rejection of the pups by the mother was discussed.
- The fate of the animals from the breeding Protocol not being used for regulated procedures was discussed. A large amount of animals can go back onto the breeding protocols.
- 4000 animals are being requested for use over the four Protocols. The numbers for each protocol are not additive as the majority of mice in Protocol 2 will go on for continued use in Protocols 3 or 4.

Revisions:

- Cat A form states 4000 mice will be used, NTS states 3000 mice to be used, however number from protocols is 7000. Please can you check the numbers and ensure they are consistent across all documents.
- Page 5, Regarding the humane end point for if weight loss approaches 50% of sex matched littermate controls. As discussed in the meeting please reword this to make it clearer that this is a measure of the ability to thrive.
- On page 6, in the reduction section 3000 mice are stated as being needed, but the estimation states 2000 are needed for colony maintenance, and a similar number for experimental protocols - this equals 4000. Please can you check the numbers (see earlier comment above).
- Page 6, please can you include some information on what constitutes success in vitro – i.e. how do you determine if a vector is suitable for in vivo use?
- Page 10, 5th sentence down - "time" should be "team".
- Page 14 – please correct the 7th line of section 'How do each of these objectives relate to each other and help you to achieve your aim?' "This platform of biological understanding will use used to design the therapeutic strategy"
- Page 23, Section 'Why are you proposing this severity category?'. Please expand on the sentence 'The risk is low due to the sterile nature of the animal facility.' What is low risk?
- Page 23, states that "experiments will follow ARRIVE guidelines". This is not quite correct. ARRIVE are not guidelines on how to conduct research. They are guidelines on how to report research that was previously conducted. Please re-word. This appears in a number of places on the licence – please re-word all relevant sentences.
- Page 25, Section 'Which general types or strains will you be using and why?'. Please check the wording of the sentence 'These include mouse models of urofacial syndrome, a disease is characterised by bladder voiding dysfunction…'.
- Page 36, Protocol 3, please check with the BSF if all the steps in Protocol 3 can be optional or if one has to be mandatory.
- Page 37, Step 3, please expand on how renal function will be estimated by measuring substances in the blood in consultation with the BSF staff.
- Page 39 and 51, should cytometry be cystometry?

- Page 42, the experimental design is not determined by a regulatory guideline - as the applicant answered yes a number of experimental design questions are now missing, such as sample size calculations, choice of control groups etc. Please can you select no and complete the questions that are populated.
- Page 43 and Page 55, I'm not clear what following NC3R experimental design means. Please can you clarify this.
- Page 47, Section 'Describe the procedures that will be carried out during this step.' Please correct the sentence 'For intravenous administration in the first or second day after birth ups will be removed from the mother and general anaesthesia will be induced by an inhalation agent' to say pups.
- 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]
    - Generally easy to read, but a little long perhaps and some technical language which could be discarded, please see below for examples.
    - "viral vector mediated gene therapy" is not appropriate for this point in the NTS - needs putting into non-technical language. This also applies to "viral vectors are used to deliver therapeutic transgenes", "molecular pathology"
    - "faithful animal models" - use of "faithful" here is obscure to non-technical readers [c.f. also p.4, p.6]
    - "Typically what will be done" paragraph is in one way quite clear, but it has several technical terms that are not at all clear, e.g. - "heterozygous mutant parents … 1/4 homozygous", "systemic injection", "in vivo cystometry". This also applies to "expected impacts".
    - Page 6, "Which non-animal alternatives" paragraph: "the ability of each viral vector to drive expression of the therapeutic gene in a relevant cell line" needs translating for non-technical reader.
    - Page 8, please reword "they faithfully model the urofacial syndrome bladder voiding disease (as other groups have for genetic mouse models of Chrm3 and ChrnA3 mutations)" for a non-technical reader.
    - Page 8, it may be better presented as "we" as in the research group "we" will regularly check the NC3R website, stay informed, etc. The we feels more inclusive and indicative of a culture of care.

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

3.2. [redacted], Modelling Fibrosis in Multiple Organs to Understand Disease

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

Interviewed: [redacted]

Discussed:
- The committee discussed the guidance from the Home Office about the percentage of weight loss that is generally allowed under the mild, moderate and severe severity bandings.
- The committee asked for how denial of permission for the severe protocols would affect the overall aims and objectives of the application.
- It is a big licence with a large number of Protocols.

Revisions:
- During the meeting you discussed a new scoring system which you are looking to adopt. Please include this scoring system with the revisions. If the use of this scoring system does not pick up night-time deaths then you will have to implement a night-time monitoring regime after discussion with BSF staff.
- Please can you check the full application for typographical errors.
- Please can you describe if you are looking to phase out sham operations.
- Please can you state if your group already has expertise of the different surgical procedures on this application and if not, how will this expertise be sought.
- Page 14, In "Lung Fibrosis" the term ILD needs to be defined.
- Page 23, Under Protocol 11, the penultimate sentence does not make sense. Please re-word.
- Page 47, please can you re-word the term 'lung delivery'.
- Page 49, Under "What are the likely adverse effects" the final sentence of paragraph 1 says minipup and not minipump. This is repeated in each section thereafter. Please amend.
- Page 54, Is the oral administration of glucose via gavage? If so, please include this in the sentence.
- Page 83, please update the 78mls/kg to be 7.8mls/kg.
- Page 94, please explain what DEN is.
- Page 95, a reference for "Workman et al" would be useful (penultimate paragraph).
- Page 107, please clarify what IVIS is.
- Page 138, please clarify what YAP signalling is.
- Page 180, please check that this is not a repeat of the calculation on 158.
- Page 204, please check the power calculation on this page.
- 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 3, "novel dynamic markers of disease" would be better reworded for the non-technical reader.

- Page 4, "mice share approx. 86% gene homology with human whereas rats share around 94% genetic homology" would be better reworded for the non-technical reader.
- Page 5, "the animal will be put down". Please change to the animal will be humanely killed.
- Page 6, “Phenotypically” is not a word that may be instantly understood by a lay reader. Please consider if it could be deleted from NTS without loss of meaning.

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. 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.

Discussed: The amendment is a refinement for how blood will be collected on two of the severe protocols of the licence.

Revisions: None

Outcome: The amendment was given approval.

5. Report on licences processed from 06/05/2021 to 06/2021

The following amendments were approved by the executive committee.

5.1. Amendments to Project Licences

[redacted], Understanding Vision & Developing Therapies for Blindness
[redacted], MK2 as a Regulator of Inflammation in Alzheimer’s Disease
[redacted], Neural Basis of Tactile Behaviour
[redacted], Genes and Essential Nutrient Influences on Behaviour
[redacted], Generation, Breeding & Maintenance of Genetically Altered Rodents

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

[redacted], Generation of mNLS Mouse Line Using CRISPR

5.3. Applications for Category C work

[redacted], Role of Frontotemporal Dementia-Associated Mutations of CHMP2B in Regulation of Synaptic Function

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

6.1. [redacted] licence has been granted. Licences from [redacted], [redacted] and [redacted] have been submitted to the Home Office following revision of the licences based on the comments raised by AWERB.

7. NACWO report

7.1. Water pouch incident
A new colour-coded system has been introduced which gives a clear indication which pouch needs to be checked 24 hours after the new pouch has been placed on the cage. SOPs have been updated. The Home Office issued a letter of reprimand which is the mildest form of reprimand that can be given. Monthly audits will take place and the results of these shared with AWERB.

7.2. Four new NACWos will be starting.

7.3. A pre-checklist for anaesthesia has been created for use before the machine is used. A service has been carried out.

7.4. A new system has been purchased to monitor temperature in the rooms which will provide alerts via SMS/email or phone or all. This system is independent from the estates system and will notify BSF staff directly. Estates have been provided with a flow chart and contingency plan for when they receive alerts from the Building Management System given the failure to contact BSF previously.

7.5. The Chair noted all the changes that have taken place and appreciates the implementations.

8. NVS report

8.1. A report was submitted to the committee containing updates from the NVS.

9. Standard Conditions 18s

9.1. The system for notifying the Home Office of Standard Conditions 18s has changed. No inspectors being assigned to establishments. Instead, a group of Home Office Inspectors are tasked with receiving Standard Conditions 18s.

10. 3Rs AWERB subgroup report

10.1. The second meeting took place on 23 June and reviewed the backlog of retrospective reviews. The sub-group considered 7 review and 3 people attended in person. Small changes were identified to the review forms which have been made. The Chair thanked [redacted] for setting up the group.

11. NC3Rs Regional Programme Manager update

Funding

1 - [redacted], partnering with University of Pisa, has been awarded a Skills and Knowledge Transfer grant. The title of [redacted] project is Replacing in vivo models with the Quasi vivo system to investigate metastatic site priming by tumour cells.
2 – 1 Project Grant application from the University of Manchester has been invited to the final, full application stage by the NC3Rs (there were 22 invitations issued in total). The panel meets next month with results announced at the end of July.
3 – 5 applications were also made to our Studentship call this year (the total number was 103). The application deadline is mid-July, with results expected to be announced in October.

Events
4 – The Manchester 3Rs symposium will be held next week – unfortunately due to the low number submitted the poster competition has been cancelled. However, we do have some great talks lined up so please do register and encourage members of your group to come along.

Resources
5 – The NC3Rs have launched a new resource this week aimed at technicians – it will help them decide how to best evaluate new environmental enrichment to determine if they are beneficial to animal welfare. You can access the resource here.
6 – A new webpage focusing on severe suffering has been launched by the RSPCA. This new website offers practical information and support on topics such as welfare assessment and humane endpoints, to help anyone involved in animal research put this key aspect of refinement into practice.

12. Any other business

12.1. The Chair thanked [redacted] and [redacted] in their absence for all their work in the time they were NVSs at the BSF.

The next meeting will be on 19 August 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
30 September 2021