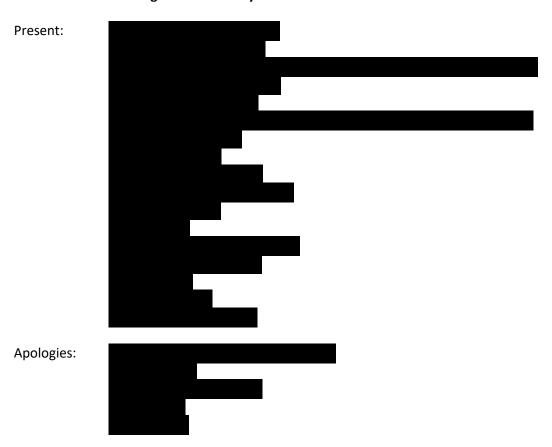


The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 27 May 2021



1. Minutes

Agreed: That the minutes of the meeting held on 15 April 2021 were approved.

2. Applications for New Project Licences

2.1. , Targeting the Tumour Microenvironment for Anti-Cancer Therapy.

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

Management Committee Meeting

Interviewed:

- *Discussed:* The committee discussed that the applicant had overestimated numbers of animals experiencing sudden death in protocol 3 and the number of times an animal would be anaesthetised for imaging.
 - A discussion with the applicant took place regarding the types of cancer in the licence.

Revisions: • Please clarify in Protocol 3 that the mice will only undergo one tumorgenesis step out of the 3 potential ones listed (tamoxifen to induce tumours in GM animals, application of carcinogen to skin or

- transplant of tumour cells/pieces via s/c, i/v or stripped mammary fat pad.)
- Also in P3, all specific adverse effects and humane end points relating to tumour growth (volumes, ulceration, impairment of normal behaviour etc.) seem to have disappeared from this draft. Please reinclude them.
- Please discuss the use of anaesthesia with the BSF staff. Animals are
 not routinely anaesthetised for scanning unless it is really needed.
 The committee expressed concerns that in the current draft you state
 that "The maximum number of times an animal may be anaesthetised
 in its lifetime is 26".
- In protocol 3, you state that up to 5% of 7000 mice may suffer from sudden death. The committee felt this was a large number of animals and require you to amend the licence to reflect the fact that in the meeting you explained that you were meaning that up to 5% may exhibit ill health, not just sudden death.
- On page 51 Step 7 of Protocol 3 Please can you consider constraining these options so as not to allow such intensive insults to the mice. For example, please include text to explain that no mouse will experience worse than 'x, y, z'.
- Please include that you are going to measure tumour size with calipers.
- Page 45 please consider rewording the last paragraph to make it clearer.
- Page 46 please include a reference for the body condition score you refer to.
- 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

who will be happy to interact with you in generating a suitable NTS.

As mentioned in the meeting, please use your presentation as a template for how to revise your NTS. The NTS should be written in a language that a non-scientist can understand. You may find it beneficial to look at examples of NTSs previously approved by the committee:

https://www.manchester.ac.uk/research/

environment/governance/ethics/animals/research/

TITLE - 'Targeting the tumour microenvironment for anti-cancer therapy' - I wonder if you might want to rethink the title so as to give a better sense of what the project will be doing in lay language - specifically could the word targeting be changed to another verb or explanation that better conveys the purpose of the project? [this is a suggestion as targeting does not make a lot of sense on its own on first impression - though it begins to

- make sense as one proceeds into the NTS; in the subsequent aims section the word 'understanding' is used which does make sense to a general readership on first encounter]
- On Page 3 please explain what is meant by stromal elements
- Please reword the NTS to explain what you mean by the terms supportive tissue environment, immunohistochemistry, immunoblot images, quantification of mRNA levels, expression of growth promoting oncogenes, null mutations of tumour suppressors, EDAR hyperactivation, enteral or parenteral: these are all technical terms that need clarification in an NTS which is for a lay reader.
- Particularly in the Reduction section, there is far too much detail for the NTS reader, and the example of a breeding schedule on page 8 is not presented in such a way as to be comprehensible to the non-specialist.
- Expected severities should be described without referral to the Protocols as these will not be evident in a 'stand-alone' NTS document.
- Page 5 and 6 Just say: mice will be humanely killed rather than a full paragraph on schedule 1 methodology.
- Page 5 oral gavage, "exsanguination via cardiac puncture", "perfusion with fixative" etc. would be better rendered in lay language if possible.
- Page 5 a brief mention of oral gavage would be helpful as would the stress due to restraint and transient discomfort from needle insertion and blood collection.
- Page 6 "The overall health of mice bearing benign tumours is generally acceptable" - might it be better to say is not anticipated to cause suffering? 'acceptable' is a bit vague and readers may have different views on this. However, a statement of not suffering would be clearer.
- Page 6 What are the expected impacts and/or adverse effects for the animals during your project? - In the first line do you mean "benign"? Most of the tumours you are studying are malignant.
- Page 7 The information describing the Protocols is not required in an NTS.
- Page 8 "How have you estimated the numbers of animals you will use?" This section is too long. Please shorten it to a few sentences and remove the diagrams.
- Page 9 The 'What steps did you take during the experimental design phase to reduce the numbers' is too long and can be cut substantially.
- Refinements section There could be more on good handling techniques and a mention of how imaging will use radiation doses that have been shown to cause no harmful effects to the animal.

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. , Immunomodulation in Cancer

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

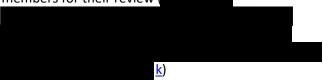
Interviewed:

Discussed: •

- The work was initially submitted as an amendment. The applicant listened to the advice of the BSF staff and revised this to a new licence application which incorporated the suggested changes.
- The applicants will be looking at the effects of graphene oxide as one
 of the immunomodulators and if using this as a scaffold changes the
 uptake into the immune cells.
- The applicant gave a very clear presentation.

Revisions: •

- In several places there is mention of a score sheet developed with the NVS and NACWO. Please include this somewhere in the application if it is not a standard score sheet.
- Page 6 Under which non animal alternatives have been considered please remove zebrafish.
- Page 25 Under "What proportion of animals will experience this severity" you say that for the majority of mice it will be mild. Please be more specific that 'majority'.
 - 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



- TITLE: is it possible to express the title without the word Immunomodulation or with some gesture toward its meaning for the lay reader? Perhaps something like "modulating" or "Using" the immune system for cancer therapy. The title is the first thing a lay reader will see and forms part of the NTS.
- Immunomodulatory needs explaining at its first appearance in the NTS.
- Page 3 "are refractory" could this be said more simply, nonresponsive maybe?
- Page 4 The reference to the Protocols is probably not relevant , particularly as the NTS should be able to seen as a document in isolation.
- Page 4 Minor typo: delete 'on' in 'through on our fundamental research'
- Page 7 Please revise the wording of "we use antibody blockade of wild type mice, instead of gene deficient mice" for a lay reader.

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. Cat C application

3.1. The evolution of adrenergic regulation of heart performance: a comparative perspective

Considered: A Cat C application form. Project overview.

Interviewed:

Discussed: •

- Cat C applications are usually considered by the executive committee of AWERB however given the species being used and the original sourcing of the animals the application was submitted for review by the full AWERB.
- The BSF had not received adequate notice of the application and was not involved early enough in discussions about the procedures to be undertaken in the BSF. The applicants were notified that the BSF should be contacted as soon as possible when planning any future work.
- has visitor status at the University of Manchester so is governed by its policies and procedures.
- The applicant has been in touch with other researchers regarding the sharing of tissue.

Outcome: The study was given approval based on the following provisos:

- All animals used on this project MUST be purchased by BSF from with whom BSF have now established an account. No animals are to be purchased outside of this arrangement from or any other source.
- For each animal type described in the application, when the concussive Schedule 1 killing is used to for the first time, it will be observed by a NTCO and NVS to ensure compliance and competency.

4. Report on licences processed from 26/03/2021 to 05/05/2021

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

, The Long-Term Effects of Developmental Hypoxia on Cardiac Function

, Understanding The Role of Inflammation in Dementia
, Extracellular Matrix in Development & Disease
, Fish Physiology in an Era of Climate Change
, Understanding Inflammasome Dependent Inflammation

4.2. Amendments to Project Licence ; Generation, Breeding and Maintenance of Genetically Altered Rodents

, Generation of RelA-HaloTag Mouse Line Using CRISPR

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

- 5.1. licences have been granted.
- 5.2. licence has been returned from the HO with minor revisions.
- 5.3. will not be attending the July meeting as their funding application was not successful.
- 5.4. have revisions to make and have been told they may not be able to attend the July meeting if they do not submit the revisions in a timely manner.
- 5.5. The August meeting already has two PPLs pencilled in for considered but a third may need to be added relating to secondary availability changes.
- 5.6. The September and November meetings may have to consider three PPL applications. This is not due to people not adhering to timelines, but new members of staff starting who require project licences.

6. NACWO report

- 6.1. The was a major failure of the heating potentially caused a lightning strike. Estates and Security failed to notify the BSF staff. Meetings have taken place regarding the communications failure given the potential adverse impact on the animals in the unit. The Deputy Director will provide an update at the next meeting. The PEL was notified of the issue immediately. The BSF are looking to update the Building Management System (BMS) and looking into options of receiving text message notifications directly should the system flag an issue.
- 6.2. There has been no feedback from the Home Office about the watering issues or the submitted Standard Condition 18s.

7. Research Compliance Committee report

- 7.1. The report submitted to RCC was provided for the committee. No comments were
- 7.2. The BSF submitted their annual report which goes to the Board of Governors. All areas of compliance that report to RCC submit an annual report which are included as appendices in the RCC annual report.

8. NVS report

8.1. A report was circulated to AWERB. No comments were made.

9. Standard Conditions 18s

- 9.1. The committee discussed the SC18 relating to the attempted anaesthetisation of a sheep after the issue with the machine was thought to have been resolved. The point was raised that before any procedure takes place the equipment should be checked as standard. The NVS reported that the issue with the machine was not obvious to the engineer. The HOI has interviewed all parties involved. Steps are in place to ensure it doesn't happen again.
- 9.2. The point was raised that there appears to have been an increase in SC18s. The NVS reported that the Home Office view SC18s as a positive action.

10. Any other business

10.1. Revisions to AWERB Terms of Reference and Operational processes documents to include 3Rs subgroup and final versions of the documents for the 3Rs subgroup (for information only)



raised the point that the NTSs are difficult to find on the external facing website.

The next meeting will be on 8 July 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