MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 19 October 2023

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 21 September 2023 were approved.

2. **Applications for New Project Licences**

2.1. [redacted]**, Anti-cancer therapy validation**

Considered: A completed AWERB form and PPL application

Interviewed: [redacted]

Discussed with applicant:

- Clarification is required regarding the Body Condition Score scale.
- The use of only one sex of animals was discussed.

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.

- There are a number of typographical errors throughout the application that should be corrected before submission to ASRU.
- Please provide the body condition score sheet which will be provided to the committee for information. The following text was unclear either due to an error or because the BCS sheet would clarify this:
  - (c) Body condition score of <2 or weight loss of 20% would indicate immediate cull (schedule 1 method or exsanguination/perfusion fixation under terminal anaesthesia with killing completed by schedule 1 method).
  - (d) Body condition score of >4 would indicate immediate cull (schedule 1 method or exsanguination/perfusion fixation under terminal anaesthesia with killing completed by schedule 1 method).
- In protocols 1-6 there is discussion of using sham surgery as controls. However, the mandatory step in each protocol probably doesn't cover sham administration of tumours - can you check this?
- Page 24 - Can you clarify whether for non sex-specific tumour types (i.e. not endometrial, cervical, prostate) you will be using both male and female animals? Can you comment on the validity of only using one sex of animals if not?
- Page 25 - Does the transgenic mouse NSG need to be defined? It does not say anywhere what it is. This is the same for other the protocols.
- Page 28 - For HEPs - I assume animals are culled if any of the points are reached. The first 2 are not labelled but 3rd/4th labelled a) and b) - so it is not clear.
- Page 30 - Is there a time frame for how long you leave animals after oestrogen withdrawal to assess if their symptoms reverse?
- Page 43 - You state that "dose levels will generally have been established to be below MTD but above those required for biological effectiveness based on studies conducted outside of the PPL (ascertained via literature, through collaboration or CRO) and refer to the guidelines in Laboratory Animals(2001)35, 1--41. I wonder whether there are any circumstances in which tolerability will need to be verified with your own mouse strain and husbandry rather than relying on third-party work under possibly different conditions, and whether this is fully covered by the PPL. Please seek advice from the BSF about this.
- Page 49 - Have you considered other ways to ensure the person measuring the tumour size/any other outcomes can be blinded to treatments? Can cage cards be altered or animal IDs be edited and matched up post-analysis, or treatments blinded/coded?
- Page 53 - For HEPs are a, b and c all the same?
- Page 120 - do you see increased pain symptoms in animals with bone tumours compared with lung/systemic tumours, given this is the most

painful cancer location in humans? If yes should there be any differences in the treatment/endpoints/severity for protocol 5?

- 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]
    - Using the mice who haven't grown tumours as company for mice remaining on study is a lovely idea and possibly something many researchers might not think important enough to add to the NTS, though I do feel it is very relevant.
    - Page 3 "What's the aim of this project?" I found this an almost impossibly dense single-sentence paragraph, and I didn't see what was meant by "data that either drives forward or stops progression of 3-5 anti-cancer therapies". This initial paragraph should help the non-technical reader into the remainder of the NTS - I don't think it does this. Some brief explanation of just what is meant by "proof of concept data" would also be helpful.
    - Page 4 - [first paragraph] The first sentence seems difficult to follow from "and enable 'no-go' decisions to "...novel approaches."
    - Page 4 - In response to the question "How will you look to maximise the outputs of this work? For example, collaboration, dissemination of new knowledge, or publication of unsuccessful approaches" the applicant responds: "...Resources will be made available to other researchers (e.g., data, animals, tissues) to enable collaborative work." Please describe how access to such resources will be managed and facilitated, with reference to the FAIR principles www.go-fair.org. For example will the imaging data be uploaded to an XNAT database somehow?
    - Page 5 - Please do let Mike Addelman know if you make any progress with the complex in vitro systems you are developing and we shall publish an item on the 3Rs section of the external facing website.
    - Page 5 - "Typically, what will be done...?" While I note that this section is headed "typically", I would want to know what else alternatives might be involved in the two instances where "for example" is used. And what sort of 'appropriate interventions' are referred to in the final sentence?
    - Page 6 - "Replacement" This is the NTS, and the terms in vitro, in vivo and in silico need explaining, (I note that in vitro and in silico are explained in the subsequent paragraph) as do pharmacokinetics and knock-out or over-expression studies.
    - Page 7 - "Reduction" 'From this, we have estimated the number of mice needed to deliver the package of data for go/no go decision making to take 3-5 novel therapies/treatment strategies to the clinic.' I think I know what this sentence is saying, but I'm not certain. Please can you consider rewording.

- Page 6 - Regarding reduction, have you considered the use of sequential or adaptive designs, particularly in settings where there is a risk of adverse effects of metastasis?
- Page 8 - paragraph beginning "Pilot studies" includes terms that are not clear to the non-technical reader - e.g. 'metastatic potential'.
- Page 9 - "How will you stay informed" This is the NTS: a list of technical acronyms doesn't help the non-technical reader.
- Page 9 - "How will you refine" 'viable and non-viable regions' - unless I've missed something, this is the first appearance of these terms, and needs some sort of explanation.

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], Parasitic helminth infections: mechanisms of immunity and immunoregulation

Considered: A completed AWERB form and PPL application

Interviewed: [redacted]

Discussed with applicant:
- The applicant explained why Protocol 2 is categorised as moderate when 99.9% of the animals will experience mild degrees of suffering. This is to take into account the duration of the mild suffering.
- A discussion about the humane end points took place.

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 check the numbers on the protocols add up to 18000, and not 17500.
- Page 38 - Minor thing but wondering why table used in one protocol but not the other (for administration of substances)
- Page 40 – Please explain why the HEP are different for parasites administration between protocol 2 and 3, e.g. 15 versus 20% body weight loss - protocol 4 also 20%
- Page 40 – Does an 'administration of gene inducers/cell depleting substances' step need to be added to protocol 4?
- Pages 42 and 51 - Anaesthetic code for gavage missing - I think
- 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 – Maybe add media engagement in the NTS under outputs?
  - Page 5 - Could you explain a little more about the faecal transplantation via oral gavage on P5 under what will be done to the animals? I am assuming oral gavage is the least stressful way to give a faecal transplant?

- Page 5 - Are you studying the effect of both male and female whipworms?
- Page 7 - This is such a clearly written NTS that I hesitate to point out that "oral gavage" [in the second line of this page] isn't a term with which the non-technical reader will be familiar.
- Page 7 - on the previous page, under "typically, what will be done..." there's no mention of irradiation, nor of bone marrow transplantation or faecal transplants.
- Page 8 - In Replacement: "epithelial tissues" needs some explaining, as does 'in vitro' (unless I've missed an explanation earlier in the NTS).
- Page 9 - In "What measures" - 'inoculum' = ?
- Page 12 - The reference to 'Freund's complete adjuvant' doesn't make sense for the non-technical reader, though it is clearly significant. 'Adjuvant' itself might also need a brief explanation.
- Overall, this is a very clear NTS, taking note of what the non-technical reader will and will not understand.

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 01/09/2023 to 06/10/2023

The following amendments were approved by the executive committee.

3.1. Amendments to Project Licences

[redacted], Regulation of Basement Membrane Function in Health & Disease
[redacted], Studying Cognitive Function in Animal Models of Brain Disorders

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

[redacted] Creation of Col4a4 Mouse Line Using CRISPR
[redacted] Creation of NLRP3 flox Mouse Line Using CRISPR
[redacted] Creation of B6.129(Cg)-Gt(ROSA)26Sort$^{m4(ACTB-tdTomato,-EGFP)Luo}$ Hamp^{Em1Uman}/J Mouse Line Using CRISPR

3.3. Applications for Category B work

[redacted], Clinical Study on Efficacy of Intranasal Spray Vaccine for Small Ruminant Against Mannheimia Haemolytica
[redacted], Effects of Photoperiod Variations on Hemiscyllium ocellatum Embryonic Development

3.4. Applications for Category C work

[redacted], Exploring Capacitive Electrostimulation For Improving Dental Implant Osseointegration

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. A report was circulated to the board members with the papers. The AAALAC response from the planned visit in November is expected February 2024. Members of AWERB are invited to meet with the AAALAC inspectors.

6. Any other business

6.1. Papers provided to AWERB – inclusion of pre-AWERB minutes or marked up PPL

A discussion took place on if the pre-AWERB minutes are still required to be provided by the BSF given the workload it takes to generate them. Alternatives were discussed including a marked up version of the PPL in addition to the final draft version but it was felt this would be unnecessary and add to the already large amount of documents the committee are required to read. Some felt it was useful to have the pre-AWERB minutes but some people did not, and felt that procedurally as long as the members trust the process has been followed and the applicant has made all the changes required from the pre-AWERB meeting then the minutes are not needed.
It was agreed to try adding a slide to the presentation whereby the applicants are asked to explain how they addressed the main points raised by the pre-AWERB members.

A related discussion took place about the procedure for ensuring the stats review happens prior to the pre-AWERB meeting or is part of it. The Secretariat will contact those people already contacted 12 months before the end of their current licence to advise they contact the statistician prior to the pre-AWERB meeting happening.

6.2. Cat C form for full committee review

[redacted], Embryonated Chick Egg Practical (Form Cat C attached)
No comments were made on this application. Approve subject to Named Persons sign-off.

6.3. Cat E new form

Following an incident with a project licence holder, the Director of Faculty Operations in FBMH asked for a process to be devised for undergraduate teaching involving animals. Staff in the BSF submitted a proposed Category E form. The proposed procedure and form needs to go through due process before it can be implemented. Consideration needs to be given to if the proposed person to administer it is appropriate.

6.4. Animal research debate

Being held on 28 November 2023, the panel, which will be debating questions from the audience, consists of Wendy Jarrett CEO of Understanding Animal Research (UAR), Penny Hawkins Head of the Animals in Science Department, RSPCA Science and Policy Group and Celean Camp from CEO of the Fund for the Replacement of Animals in Medical Experiments (FRAME). AWERB members are very welcome to attend if they

wish, and they are welcome to pass on the link to any colleagues or students they feel might enjoy the debate. Attendees are also asked to send their questions they would like panel members to debate to animal.research@manchester.ac.uk

6.5. Podcast

This is moving forward and the journalist has begun to interview AWERB members.

6.6. [redacted]

[redacted] is standing down given his new role as Vice Dean for Research and Innovation in FBMH. The Chair thanked [redacted] for all his work on AWERB.

6.7. Workload planning

In FBMH, AWERB is being included as part of the workload. The Chair hopes this is taken up in the other Faculties.

6.8. NVS

Whilst not on the rota for the agenda, the NVS reported that they have seen nothing to concern them on recent visits.

The next meeting will be on 16 November 2023 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