The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 23 February 2023

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. Minutes

Agreed: That the minutes of the meeting held on 26 January 2023 were approved.

2. [redacted]

[redacted]

3. Applications for New Project Licences

3.1. [redacted], Targeting Parasitic Helminths With Drugs

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

Interviewed: [redacted]

Discussed with applicant:

- The inclusion of Protocol 2 and the harms associated with this was discussed it the context of avoiding greater harms in Protocol 3.
- The sex of the mice being infected was discussed with the researcher clarifying that males are used initially but once a tolerable compound is found the work is carried out in box males and females.
- The use of mash earlier on was discussed in relation to mitigating weight loss. Mash is usually given at the first sign of weight loss.
- The researchers will aim to reduce the number of blood samples as they obtain data.

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.

- General comment: I personally found the use of the toxicology-related terms in the tolerability work (Protocol 2) such as "non-toxic" and "toxicity" slightly misleading, since the proposed procedures are (rightly) very far from being meaningful GLP toxicology studies in rats.

I suggest using only "tolerability". This is a personal preference, though.

- Page 16 – please can you include an explanation of the abbreviation 'STH'.
- Page 32 and 41 – please check this as there appears to be a discrepancy in number of doses when given i.p. The text states no more than twice daily for 2 days but the table state 5 days.
- Page 45 – please consider revising the wording of the first paragraph to make it clearer.
- Page 48 – in the section 'Why can't you achieve your scientific outputs with an earlier humane endpoint, or without animals showing any clinical signs?' there is a typographical error which should read 'humane endpoint'.
- 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]
    - This is a very clear NTS - to be commended for its presentation for the non-technical reader.
    - Though the NTS is a little long in places and there is some repetition, it is clear, comprehensive and reasonably easy to understand from a lay point of view. Minor points: I would just use 'novel chemical substances' in the NTS, rather than 'novel chemical entities (substances)'. Perhaps add that many of the mice will be severely immunosuppressed and therefore kept in sterile conditions?
    - Could 'chemical entities (substances)' be one word that remains the same throughout giving consistency?
    - Page 2- please consider if the word 'clear' could be replaced by 'eradicate' or 'remove' or 'get rid of'.
    - Page 3 - you say the primary output of the project is to identify up to 5 compounds which target parasitic worms in vivo however on page 18 and page 37, you say that objective 3 is to identify 2-3. It might be good if the wording is consistent. Alternatively, could the number of compounds required be removed so that it reads 'to identify novel or repurposed compounds'.
    - Page 3 - Typo in Benefits - share our findings.
    - Page 4, 8, 10 and 57 – please can you change 'man' to 'humans' based on the assumption that the worms infect both genders.
    - Page 5 – please define 'cytotoxicity'
    - Page 6 - In 'in vitro screening' paragraph the term 'assay' first appears without any explanation for the non-technical reader - unlike just about every other term, which you have been careful to introduce/explain – please can you include some explanation for this word.
    - Page 6 – please can you include a brief explanation of what 'free-living mode' means.

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], In Vivo Studies of Pathways & Cells Involved in Detecting Damage & Commensal Microbes to Elicit Cancer Immunity ([redacted])

Considered: PPL application and minutes from Local Management Committee Meeting

Interviewed: [redacted]

Panel discussion:
- A presentation will not be given as the application has been seen previously and is being reconsidered after revisions.
- Since the application is an additional availability, only those protocols that relate to the BSF will be considered.
- Statistical input has been sought in house from [redacted].

Discussed with applicant:
- The practicalities of working in a germ free facility need to be considered and advice from the specific BSF staff responsible for this environment should be sought before the studies start. Working with germ free mice is labour intensive.

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.
- Page 54 and 165 – please can you explain what the abbreviation MGS means.
- Page 165 - Humane end points for the induction of cancer seem in complete to me. They only consider tumours that can be seen and measured which will not be the case for those in the intestine (induced by Step 1 2b). How will the investigators safeguard welfare with these animals - especially as they say diarrhoea cannot be used as GF mice already have watery poos.
- Page 166 - It is not clear when the therapeutic agents are given how the GF, or mono colonised mice, will be anaesthetized? A number of the procedures are listed as AA/AB.
- Page 167 - are there really no possible adverse effects for the administration of a therapeutic agent? I.e. step 3? (this comment applies to all protocols)
- Page 167, 168, 185, 186, 187, 202, 203 - b and d are the same – is this an error?
- Page 168 - are there really no possible adverse effects for the administration of a therapeutic agent? I.e. step 4? As with the point above this doesn't seem correct. Surely there are risks associated with both the method of administration and also the agent being administered? (this comment applies to all protocols).
- Page 169 - Under "What are the likely effects….." there is a typographical error as it should read "transgene".
- Page 170, 188, 205 – please consider including an explanation for the abbreviations eGFP, RFP.
- Page 181 - adverse effects of immunisation just mention "loss of condition", What about risk of granuloma or abscess formation?

- Page 187 – please explain the abbreviation FCI.
- Page 190 – please seek advice from the BSF if the phrase 'insulators' correctly describes where the animals are kept.
- Page 190 – you refer to step 10 but this does not appear to be listed.
- Page 199 - Adverse effect of DSS listed as diarrhoea - but its already been stated that in GF mice this is an issue as mice already have soft faeces. Does this relate to re-colonised mice only? And if so how will diarrhoea be used to compare severity and condition of colonised and non-colonised mice?
- Page 207 – please can you double check the steps listed.

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], Cellular Homeostasis & Brain Development.

Considered: A Home Office amendment summary sheet and highlighted amendment Project Licence.

Interviewed: [redacted]

Panel discussion:
- This amendment has come to the full committee as it was felt the requested additional work was over and above what was approved previously.
- The licence is already granted so comments on the NTS and typographical comments not relating to the added Protocol will not be provided back to the licence holder.
- The NVS reported that while the technique seems invasive is actually isn't and is very simple and well tolerated.

Discussed with applicant:
- The licence holder is experienced in the procedures listed in the additional protocol.

Revisions:
- page 79 please update the sentence so it reads 'Although mice are known to be good swimmers, in the event that a mouse is ***in danger of*** drowning, it will be rescued immediately and removed from any further behavioural tests.

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

5. Report on licences processed from 12/01/2023 to 08/02/2023

The following amendments were approved by the executive committee.

5.1. Amendments to Project Licences

[redacted], Immunoregulation During Parasitic Helminth Infection.
[redacted], Biocompatibility of a Prototype Fully Implantable Auditory Implant Microphone.

[redacted], Circadian Regulation of Chronic Inflammation

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

[redacted], Creation of C57BL/6J-Tnfaip6^{E183S}/Day (or TSG-6^{E183S}) Mouse Line Using CRISPR

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

6.1. The committee were provided with a document showing the status of applications considered previously and those pencilled in for future meetings.

7. NACWO and Directors report

7.1. No comments were made on the report submitted.

8. Any other business

8.1. AWERB / RSPCA meeting 12th May - Maximising the Effectiveness of your AWERB

[redacted]

The next meeting will be on 23 March at 10am-12.30pm.

Dates of meetings for the 2022/2023 academic year are:
23 March 2023
27 April 2023
25 May 2023
22 June 2023
20 July 2023
August break

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