The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 27 February 2025

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 30 January 2025 were approved.

2. **Applications for New Project Licences**

2.1. [redacted]**, Neuroimmunometabolism: Understanding Brain-Body Communication in Health & Disease.**

Considered: A completed AWERB form, PPL application and presentation.

Interviewed: [redacted]

Committee discussion:

- The Chair invited members to raise areas of concern or clarification which were subsequently discussed with the applicant.
- The committee decided which of the pre-submitted questions or points of clarification could be addressed in the feedback letter and which they wished to discuss in person and in depth with the applicant.

Discussed with applicant:

- The committee highlighted the usefulness of videos and diagrams in the applicant's presentation. It was suggested that they could be used on an anonymised basis in communications.
- The 'writhing test' has been removed, but the applicant should make sure that all references to this test have been removed from the application, particularly in the adverse effects and animal experience section of Protocol 5.
- It was noted that the applicant had explained the use of single sex as helping to isolate the effects of specific treatments, as there are differences in hormonal cycles and physiological responses. The committee questioned in which specific protocols single sexes are being studied and which sex they are. The committee also raised concerns about a particular sex being under-studied. The applicant explained that the protocols are broad and may contain many experimental scenarios. The applicant confirmed that they do not think any sex is under studies, as both males and females used at different points as part of the funder's requirements. The committee suggested to clarify how each sex is used in the studies in the experimental design section.
- The committee asked the applicant to clarify whether 'food deprivation' was the complete withdrawal of food for up to 48 hours. The applicant confirmed this and noted that this would be limited to once per animal. The applicant noted that the idea that an animal has constant access to food is not what would happen in nature.
- The committee questioned the rationale and evidence base for placing the single-housed animals in close proximity. The applicant could not provide an evidence base for the mitigation but suggested that there is some consensus that visual and ultrasound contact with open cages causes less stress for the animals, but the 3Rs website states that male mice might occasionally prefer single housing.
- The committee raised the possibility of future analysis of microbiome with the applicant. The applicant explained that while this was not their area of expertise, they understand it does have an impact on their research and they do collaborate with individuals that look at this, so there was potential for future analysis.

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.

- The licence would benefit from checking on a couple of typographical errors.

- Please ensure all mention of the writhing test are removed.
- Page 34 - In manipulation A, please can you clarify if the food deprivation occurs in one 48 hour period not shorter periods which total 48 hours and that this is distinct from the intermittent fasting of up to 24 hours over 2 to 4 weeks.
- Page 34 - In manipulation F, though you say the maximum is 30 mins, please include details on how long would you typically have to impose acute restraint stress on the mice, and how is the length of time decided.
- Page 34 – Include details as explained in the meeting that food deprivation is the complete withdrawal of all food.
- Page 39 - It appears that cannulae will remain in situ to allow for regular withdrawal of blood or CSF. Please include details of how well the mice tolerate these cannulae and if they are likely to remain in situ undisturbed. Please also clarify if the mice with these implanted cannulae will be rehoused in single cages.
- Page 43 – Please check if the body condition scored from the condition record is included in the PPL.
- Page 44 – Please clarify if you mean 'for up to 2 days at a low temp of 4 degrees?
- Page 62 - As you say 4-hydroxy tamoxifen is a far milder drug for transgene induction than tamoxifen, why are there occasions when it cannot be used?
- Page 65 - As drinking water will be replaced with saline to negate the loss of mineralocorticoid production, are the mice able to drink it as freely as the water?
- Page 65 - Glucose monitoring. Please clarify if this involves a tail prick each time. So 4 times a session.
- Page 68 – Please check the wording for ‘Burns maze' Is it meant to be Barnes maze?
- Page 71 - Administration of substances - rarely up to 28 injections. Please include information on how often this occurs.
- Page 118 - "Animals will be placed into choice chambers to assess preference or avoidance" Please can you explained what is being avoided in the choice chamber and if there are any welfare issues.
- 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 4 - Wegovy and Ozempic are brand names - is it appropriate to use in the NTS? Might the same information be conveyed in a different way such as "new medications based on seaglutide used to lower blood sugar levels in type 2 diabetes and for weightloss". We recognise that introducing seaglutide is a technical term so perhaps best avoided within the NTS and brand names have widespread recognition. Please check with [redacted] whether brand names / trademarks can be included in an NTS.
    - Page 5 – Should ‘institute’s’ be ‘institution’s’? Note sure that ‘Institutional infrastructure’ should be capitalised.

- Page 7 - Ex vivo – this is a technical term though one much used - is there a non-technical alternative?
- Page 8 - Techniques like optogenetics and chemogenetics allow in transgenic mice' is a bit technical, could you say "techniques in transgenic mice allow"?
- Page 8 - I used data from past projects' - or we? This is personal choice really as to whether you wish to present a group or an individual in the NTS. Later you use we which reads better.
- Page 8 – 'Statistical agency' - perhaps 'statistician' and perhaps 'worked with' as opposed to consulted to indicate collaboration.
- Some minor suggestions on language for the NTS: The public will not know what a one-sided test is. Perhaps add: a way to check if something is bigger or smaller than a certain value, but not both. "Homozygous" is probably not something they will know either. Maybe: "the mice will inherit two identical copies of a gene—one from each parent, so that their offspring will have the same version of that gene, ensuring genetic differences do not affect the results. Perhaps instead of 'assay' use 'test'? It would be good to explain that you will be conducting behavioural studies on the animals in the NTS - using different types of mazes etc.
- Page 9 - How long will the animals on average be kept in the metabolic cages? Is there a maximum time?

Outcome: The Chair invited members to discuss and confirm they were satisfied with the harm – benefit analysis.
The Chair invited members to discuss and confirm they were satisfied with the implementation of the 3Rs.
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], Mechanisms Regulating Local & Systemic Immunity in Intestinal Health & Inflammation.

Considered: A completed AWERB form, PPL application and presentation.

Interviewed: [redacted]

Committee discussion:
- The Chair invited members to raise areas of concern or clarification which were subsequently discussed with the applicant.
- The committee decided which of the pre-submitted questions or points of clarification could be addressed in the feedback letter and which they wished to discuss in person and in depth with the applicant.

Discussed with applicant:
- The Chair thanked the applicant for a clear and concise presentation.
- The committee asked the applicant whether they considered moving into germ free. The applicant suggested that while this was a possibility, this was not the intention in the near future, as germ free mice have a different set of immune systems at the start.
- The committee raised concern about using weight loss as an endpoint as the combination of administering antibiotics and tamoxifen could have a significant impact on weight loss. The applicant noted that in

terms of tamoxifen, it is only used to label immune cells at a certain time point and look at how they get replaced from the bone marrow. Small amounts of tamoxifen administered via oral gavage does not see a huge amount of weight loss. The applicant also confirmed that previously they have never tried to do this with combining antibiotics and tamoxifen. If the research team did see severe weight loss with this combination, they simply wouldn't continue with the protocol.

- The committee highlighted that the dose and duration of up to 5% DSS for 7 days was quite high, and this could lead to 20% weight loss and further in transgenic lines. The applicant confirmed that they typically use 2-3% but occasionally use 5% where some strains and batches of DSS doesn't work well. The committee suggested that the applicant should add in the typical use of 2-3% to make the application clearer.
- The committee questioned the types of environmental enrichment used and noted that this should be added in to the NTS. The applicant explained that they used the standard measures implemented by the [redacted]
- The Chair asked the applicant about their approach to using in silico. The applicant confirmed that they were working with data sets that look at similar markers in human samples to those seen in mice. It was previously difficult to immune profile in the circulation of mice, due to only having a small number of cells compared to that of humans. As the technology has improved, this is where the research team are trying to do computational modelling. The Chair suggested that the applicant speak with [redacted] and his team on their work in silico.
- The committee asked if the use of syringe feeding has been considered as an alternative to oral gavage. The applicant explained that this would depend on what substance is being administered, as many are quite viscous which would make giving them by syringe difficult. The applicant further explained that best practice measures are used for oral gavage including using round tips, the smallest diameter tube possible and the use of a flexible tube.

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 for typographical errors, for example on Page 11 - around - I have around and Page 14 - Macrophges – Macrophages.
- Page 11 – Please seek advice from the Named Persons on whether naming [redacted] is appropriate, although we note this section is not in the NTS.
- Page 17 - Have you considered syringe feeding as an alternative to gavage?
- Page 17 - If Ifngr2–/– mice display evidence of an altered immune response then the same experiment will be performed but utilising an alternative mechanism to block IFN-gamma activity. Please can you clarify if different mice will be used.
- Page 19 - In-silico - this stream of bioinformatics work was not clear in the NTS - it may be worth considering adding a line to the publicly

available NTS to indicate this approach and it's potential for 3Rs contributions.

- Page 37 - Several different dosing options. Please include details on how you determine which frequency to use.
- Page 40 - States maximum of 18 hour fast, but only 16 hours stated on Page 17. Please clarify.
- Page 40 - Can you explain your use of microsampling: what it is and why it is a refinement?
- Page 45 - States use of same sex - are they any situations where both sexes may be used?
- 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])
    - NTS - Minor comments: terms such as immune dysregulation, pathophysiology, knockout, etc might be difficult for the lay reader to understand. Perhaps consider simplifying or explaining them? Perhaps add, for example, that mice sweeteners will be added to the antibiotic cocktail to make it more palatable as a refinement?
    - Page 4 – “I expect to see primarily..." This is fine but you might consider 'we' assuming you are leading a team, working with animal technologists, etc, as it sounds more collaborative though the question does imply it is asking an individual.
    - Page 5 - Can "mechanistically study" be unpacked/explained for the non-expert in non-technical language? It is unclear why to identify a mechanism you require the life stages of animals you describe at present (i.e. if mechanistic study requires and explains the need for the chosen life stages this is not obvious).
    - Page 6 – ‘Systemic immunity' -depending on how you deal with systemic above this may need a little clarification for non-expert.
    - Page 6 - Moderate – approximately 25% - what is causing moderate severity? it was not clear in the description of adverse impacts - would be good to see a clear concise explanation to balance the reference to mild (e.g. DSS induced inflammation).
    - Page 7 – ‘no good' – perhaps you could use ‘not viable’ as it sounds a bit more robust and evidenced whereas good feels a little subjective.
    - Page 7 – 'my research' - again this is fine in principle but 'our' might better recognise the wider team's contributions? Below you refer to the group and move to using we.
    - Page 7 – ‘distal interactions' – Please explanation this in a non-technical way.
    - Page 8 – ‘(as is required as a PPL holder)' - I would suggest removing this as it adds unnecessary information and risks being misunderstood.
    - Page 8 - Maybe a system issue but this question appears in your text as well as in the form: 'What published best practice guidance will you follow to ensure experiments are conducted in the most refined way? We will base our approaches on the best published practises, for example those endorsed by the NC3Rs.

- Page 10 - "We will base our approaches on the best published practises" as an answer to "What published best practice guidance will you follow " is not as informative as it could be - do you not have any examples in mind or ones you have used to evidence?

Outcome: The Chair asked members to discuss and confirm they were satisfied with the harm – benefit analysis.
The Chair asked members to discuss and confirm they were satisfied with the implementation of the 3Rs.
The study was given provisional approval based on the applicant making the changes/clarifications listed above to the satisfaction of the Chair/AWERB.

3. Mid-term reviews of Project Licences requiring full committee review

3.1. [redacted], Modelling fibrosis in multiple organs to understand disease.

Considered: A completed mid-term review form.

Interviewed: [redacted]

Committee discussion:
- The Chair invited members to raise areas of concern or clarification which were subsequently discussed with the licence holder.

Discussed with licence holder:
- The committee queried the extension of the severity band, so the animals could go to the end of the project and questioned whether the licence holder could have a disease-based end point rather than a time-based one. The licence holder explained that they wanted to know the extent of the fibrotic phase was, so the severity band needed to be extended, and a disease-based end point would not be appropriate.
- The Chair questioned how we communicate to the wider public the dependence and impact of the human model on the animal model. The licence holder agreed with the societal impact of their research. The team have had lots of funding to take their work from in vitro to animals, to test cases in humans, then talking to patients. The team have worked with a PPIE company called [redacted] and it has been fantastic for the research group to see the impact they are having.
- The committee noted the close collaboration between clinicians and surgeons that has led to productive refinements beyond the norm. The committee questioned how this could be communicated so others could model it.

Feedback to the licence holder
- The progress so far on this licence seems very impressive across the board with good scientific, public and commercial outcomes thus far.
- Page 3 - It might be helpful to acknowledge how animal research has formed a basis of the ID Liver project in the project's comms https://sites.manchester.ac.uk/id-liver/ as it could be a good opportunity to demonstrate the positive impact of animals in research. Perhaps it might also be helpful to cover this as a case study on the external animal research website. Should you wish to do this please contact [redacted]

[redacted]

- Page 6 - Q. 11 Is funding - cost of research 'crisis' - limiting the scope and ambition of research?
- Page 6 – Q. 12 - how do they anticipate the use of both male and female will impact their data and outcomes? Will the results be better, worse, comparable to past or not etc.?
- Page 6 – Q. 13 - is [redacted] now confident in the procedure?

Outcome: AWERB supported continued work on this licence.

4. Report on licences processed from 16/01/2025 to 12/02/2025

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], Understanding the role of systemic inflammation in cardiovascular disease and obesity
[redacted], Vascular calcification in kidney dysfunction
[redacted], The mechanisms underpinning 'steroid' (glucocorticoid) development of obesity and diabetes

The committee were reminded that amendments made to both [redacted] and [redacted] licences were as a result of ASRU changing their definition of forced swimming. Both PPLs contained elements of what would now be considered forced swimming. Both PPLs have reviewed what they were doing and were able to identify more refined models, so the licences have removed forced swimming. ASRU processed them quickly.

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

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

5.2. One of the applications pencilled in for the April meeting has been paused, leaving space for another application to be considered.

5.3. Licence applications have been scheduled in for AWERB meetings up to September 2025. The Chair noted that this needs to be monitored so as not to cause a significant backlog.

6. Director's report

6.1. The committee were provided with a document outlining some key updates from the Director.

6.2. The Director provided an update on the low temperature incident occurring in the [redacted] at the beginning of January. A meeting was organised with the Establishment License Holder, Head of Estates, [redacted] and the [redacted] and the Director received a comprehensive report. Going forwards a series of meetings and actions have been scheduled to learn from this incident and improve Estates support to the [redacted]

Action: **The Estates report will be circulated to the committee.**

6.3. The Director noted that Head of Estates, [redacted], attended the February EAG meeting and provided assurances that estates are taking care of short-, mid-, and long-term issues faced [redacted] The Chair noted that [redacted] Establishment Licence Holder, was fully engaged with this issue and monthly meetings will be held going forward. The Chair requested that AWERB be regularly updated on progress.

Action: **The ongoing resolution of challenges with the Estates team will be added as a standing item on the agenda.**

6.4. The Director clarified that references to the implementation of Good Laboratory Practice Standards in the report would eventually apply to [redacted], but that the facility would be looking to implement this in stages.

6.5. The Director provided an update on the vermin issue, noting that [redacted] has a robust process in place for their rooms within the [redacted]. It was noted, however, that the Director cannot be held responsible for other areas of that building. The Director has asked the Estates to consider hiring [redacted] for the remainder of the building and this has been communicated to [redacted]. The Chair encouraged members who work within UoM to raise awareness of this matter in their local areas of work.

6.6. The Director, [redacted] and [redacted] submitted a proposal for a presentation at FELASA (Federation of European Laboratory Animal Science Associations). This proposal has been accepted, and [redacted] and [redacted] will present during the symposium.

6.7. The Chair noted interested in the education programme mentioned in the document and queried about the possibility of CPD opportunities for the committee. The Director clarified that the education programme was not particularly aimed at AWERB members, but rather the Animal Technicians in the [redacted]

6.8. The Director highlighted the positive compliments paid towards this AWERB committee when visiting other facilities.

7. Culture of Care

7.1. The Chair emphasised to the committee that 'Culture of Care' is now a quarterly item on the agenda of AWERB committee meetings.

7.2. The Committee were provided with a presentation conducted by [redacted] on the updates to existing 'Culture of Care' issues and upcoming plans.

7.3. The Chair stated that he would be happy for AWERB members to play a role in the [redacted] compassion fatigue subgroup. The Chair also suggested that a Culture of Care subgroup would be something for AWERB to consider in the future.

7.4. The Chair noted that EDI processes operate through the schools and expressed concern about this reaching the [redacted] staff. [redacted] confirmed that [redacted] staff can take part in EDI workshops and is happy to discuss this with the Chair separately to ensure EDI is incorporated into Culture of Care.

8. Annual review of Environmental Enrichment Guide

8.1. The committee were provided with the Environmental Enrichment Guide, a summary of the different types of environmental enrichment for the different species. This has been reviewed by the NACWOs and the NVS to ensure that the [redacted] is implementing best practice.

8.2. When asked for clarification on the term ‘chumbling’, [redacted] explained that this is where mice crumble their food pellets into dust.

8.3. The Chair noted interest in how the [redacted] is carrying out evaluation for new environmental enrichment and whether this would lead to publications. [redacted] confirmed this could lead to publication, either themselves or working with research groups. [redacted] highlighted the difficulties in proving the positive impacts of environmental enrichment. For example, looking at ultrasound vocalisations are the only way to tell if a rat is happier.

Action: **The posters on the Environmental Enrichment research will be circulated to the Committee.**

8.4. The Environmental Enrichment Guide was endorsed by the committee.

9. Process for getting statistical sign-off

9.1. The Chair confirmed that he is aware of the commitment in the Terms of Refence to get papers to committee members 10 working days in advance of a meeting but understands that in the past couple of months this has been late.

9.2. It was highlighted that often researchers view the AWERB meeting as the target for statistical sign off. To combat this, it was suggested that a deadline of the pre-AWERB meeting be emphasised with researchers.

9.3. The Chair suggested that he would discuss this outside of committee with the members concerned in organising this process.

10. ASC AWERB Hub Workshop

10.1. The next ASC AWERB Hub workshop will be taking place on Wednesday 2 April 2025 from 13:00-16:00. The theme will be "AWERBs and the thorny issue of replacement". More info forthcoming from ASC.

11. ASRU have commissioned policy advice from the Animals in Science Committee: Animal Welfare and Ethical Review Bodies and the Named Information Officer for strengthening the functioning of Animal Welfare and Ethical Review Bodies (AWERBs) and the Named Information Officer (NIO) role.
https://www.gov.uk/government/publications/commission-on-awerbs-and-named-information-officer/animal-welfare-and-ethical-review-bodies-and-the-named-information-officer-accessible

11.1. ASRU have commissioned policy advice from the Animals in Science Committee: Animal Welfare and Ethical Review Bodies and the Named Information Officer for strengthening the functioning of Animal Welfare and Ethical Review Bodies (AWERBs) and the Named Information Officer (NIO) role. Advice is sought in the following areas: best practice guidance for AWERBs, particularly relating to their duties regarding the 3Rs and training; the questions that AWERBs should ask project applicants to check that replacement methodologies have been fully considered; a review of the ASC AWERB network model to assure dissemination of leading practice; leading practice to ensure that the NIO role functions effectively at establishments, where required. See https://www.gov.uk/government/publications/commission-on-awerbs-and-named-information-officer/animal-welfare-and-ethical-review-bodies-and-the-named-information-officer-accessible . To report by Sept 2025.

11.2. The Chair suggested that this may indicate that greater emphasis on local oversight may be an emerging theme.

11.3. It was noted that the University is perhaps ahead of common practice because there is already statistical expertise on the AWERB committee and this has not always been the case elsewhere.

11.4. The NIO explained that different establishments have different expectations for their NIOs, so clarifying the role should create more uniformity.

12. Any other business

12.1. AWERB Review Update

The Chair informed the committee that it has been decided not to move forward with a consultant and conduct focussed 12-month review of AWERB practices. Instead, the Chair will lead on a sustained process of continued review and improvement to allow for constantly evolving best practice. The first item on this review agenda is addressing our annual AWERB led audit of the [redacted] in line with AAALAC expectations.

The next meeting will be on 27 March 2025 at 10am-12.30pm.

Dates of meetings for the 2024/2025 academic year are:
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
29 January 2026
26 February 2026
26 March 2026
30 April 2026
28 May 2026
25 June 2026
30 July 2026

Dates of meetings for the 2026/2027 academic year are:
24 September 2026
22 October 2026
19 November 2026
17 December 2026
28 January 2027
25 February 2027

25 March 2027
29 April 2027
27 May 2027
24 June 2027
29 July 2027