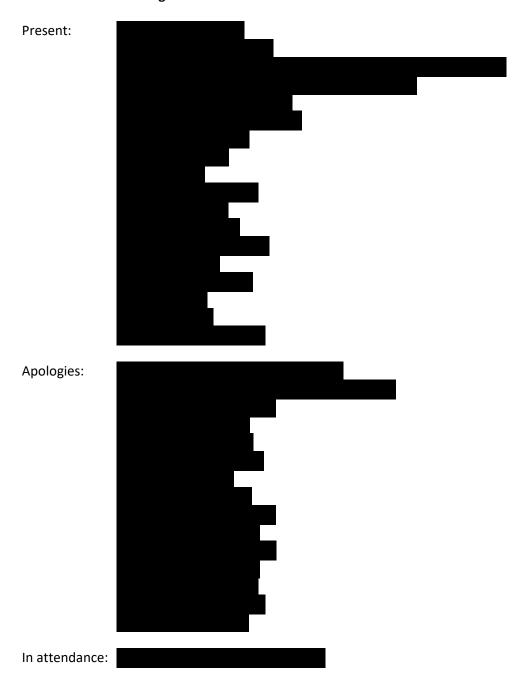


# The University of Manchester

## ANIMAL WELFARE AND ETHICAL REVIEW BODY

## Minutes of the meeting held on 12 December 2024



## 1. Minutes

Agreed: That the minutes of the meeting held on 14 November 2024 were approved.

## 2. Applications for New Project Licences

2.1. Type 2 immune regulation of repair and infection

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

Interviewed:

### Committee discussion: •

The application is difficult to follow.

# Discussed with • applicant:

- The presentation was incredibly helpful and addressed some of the questions the committee had.
- Protocol 2 why are pups left with no food and water, is this because
  the mother needs to be removed so they can be placed in the flask?
  The applicant explained that the pups survive extremely well and are
  kept in a room with high heat and high humidity. The pups are 6-10
  days old when taken from the mothers and the most critical period is
  the first week, which is why they are more likely to survive. Pups are
  used rather than adults as the adults are more likely to get rid of the
  mites
- The possibility of using sunflower seeds to encourage animals to take substances was raised.
- The wording should be checked for Protocol 3 to ensure the procedures are specific and that any cumulative procedures do not exceed moderate suffering.

Noted:

After the meeting it became evident that the version circulated to committee was not the most recent version of the draft licence. This accounted for the number and mismatch of questions AWERB had for the applicant, many of which had been raised in the pre-AWERB meeting and incorporated into the licence by the applicant. The most recent version of the licence has an NTS that is more lay, has the adverse effects better described and the humane endpoints were improved and clearer.

The comments below were determined to have already been addressed in the most recent version of the draft licence.

- Page 2 'type 2' arm of the immune system, regulates the extracellular matrix' is too technical (and has a typo). Could this be expressed in non-expert language for lay reader? NTS public document; must be comprehensible for nonexpert.
- Page 3 please can you explain what helminth infection is.
- Page 4 names should be removed from the NTS as this section of the licence is a public document.
- Page 4 consider using the phrase tiny, early-stage larvae of parasitic hookworms (if accurate), instead of nematode microfilaria.
- Page 5 What will be done to gerbils and cotton rats and what are the impacts? Presumably mild, if any? It may be helpful to have a clear line on this to remove any confusion or uncertainty.
- Page 5 Expected severity, the questions asks per type of animal.
   Your answer suggests all animals will be 85% mild and 15% moderate; is that the case (excluding breeding protocols)? So 85% of cotton rats mild, 15% moderate? If so, we need more detail on what is happening to the rats as above.
- Page 7 perhaps spell out as will not be known to non-expert reader or use animal facility as you do on p.9 (might be good to be consistent here).
- Page 51 And throughout does "weight loss approaching 20%" need to be defined - what is "approaching"?

- Page 95 Protocol 6 why is weight loss limit here 15% but 20% in others? on page 101 you mention HEP is 20%, so one of these needs to be corrected so it's consistent.
- Page 102 "Mice that receive a sufficient number of haematopoetic cells to effect complete engraftment may still experience transient weight loss, for brief periods (<48h) in excess of 20% but usually recover within 24hrs and are not expected to show anything more than mild symptoms on recovery," is this acceptable to have animals going beyond the HEP of 20% weight loss?
- Page 106 Is there a typographical error in this sentence as it mentions both 15% and 20% in same section? Why are these an HEP if observed for 72h, but in other protocols/sections if any of the symptoms are seen for only >24h it's an HEP? "Moderate severity limits are considered weight loss in excess of 15% or persistence of any of the following single adverse effects for 72h: weight loss approaching 20%, loss of condition, moderate piloerection, hunched posture, light to moderate staining around eyes and/or nose, pallor of extremities, reduced spontaneous activity and reduced response to external stimuli"
- Page 125 consider rephrasing "20 % weight loss alone 15 % weight loss or less but with other indications of reduced condition (e.g piloerection, hunching, reduced activity) for more than 24 hours" as it reads as if for an animal to have e.g 17% weight loss and other indications, that they would not have to be culled, which I don't think you intend to be the case.

Feeback to applicant:

After the meeting it became clear that the version of your draft licence that was circulated to members to review (dated 17 October 2024) was not the most recent version of the licence, which is dated 26 November 2024. We acknowledge and fully apologise for the error on our part in circulating and reviewing the wrong draft. We have identified where the mistake occurred and will take steps to mitigate the risk of any repetition.

On review of the two drafts, it is clear that the latest version greatly improves the presentation of the licence and clarifies many of the issues raised at the meeting. We now recognise that many of the concerns raised by the committee during the meeting had already been addressed in the most recent version and we regret any confusion caused by the discussion of points already addressed. We thank you for your work in responding so fully to the pre-AWERB recommendations in the most recent draft.

In discussion, the committee was pleased to see a positive commitment and clear plan for publishing 'negative' findings. We also welcomed the impressive efforts at reduction in numbers of animals for this application (by around 40% from your previous licence).

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.

- Title: could this be changed to use simpler language so the lay reader can understand it and give a sense of the purpose of the licence? Currently the title is more of a statement and quite technical.
- Page 5 to avoid confusion, please remove the mention of Cotton
  Rats in the section "Explain why you are using these types of animals
  and your choice of life stages." We suggest referring to the gerbil as
  the only suitable laboratory species or words to this effect. Mention
  of cotton rats may lead to a misreading that the project intends to
  use them.
- Protocol 2 it was unclear why the pups were left with no food and water. Is this because the mother needs to be removed so they can be placed in the flask? Could this be clarified.
- Protocol 3 Will the gerbils be re-housed together after each mite feed? Presumably they won't be singly housed for the rest of experiments, but this could be clearer. If they are to be singly housed, can you justify why as you'd expect this to have a detrimental effect on them.
- Protocol 5 Step 2 I read in the NTS that you have recently acquired transgenic mice that allow you to generate 50:50 gene chimeras without performing irradiation. I don't fully understand this can you explain it as it seems like an important refinement? Why then perform radiation in any of the mice- if that is indeed the case? Also, I understand that adverse impacts of whole body irradiation are rare, so if this is the case, no need to add that to the NTS
- A few comments were made regarding the language used in your Non-Technical Summary which are listed below. Please send the most recent version to

   ) who is a lay member on the committee and can work with you on the NTS. It may be useful to

consider the following points:

- Page 3 "Who will benefit section" is quite technical with some expert terms; it would benefit from being less technical. It is very helpful to see clarity on short term and longer-term benefits.
- Page 5-6 "Typically, what will be done to an animal used in your project?" – would it be possible to concisely clarify what will be done to gerbils and rats? Currently, the mice are clear but the others less so.
- Page 7 'We cannot perform these experiments in people, and in the rare cases where experimental human studies are performed, it is not possible to analyse the whole body response in the different tissues', would be better presented as: 'We cannot perform these experiments in people, because in the rare cases where experimental human studies have been performed it was not possible to analyse the whole body response in the different tissues.' Otherwise the sentence perhaps contradicts itself; we cannot do this in humans but it is done rarely could be confusing.
- Page 11 "What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?" Please include and refer to the PREPARE and ARRIVE guidelines.

 In the NTS, you might want to add a bit more detail into the refinement sections on provision of analgesia, antibiotic cover to prevent opportunistic infections after irradiation, general post op care, enrichment etc.

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

# 3.1. Immunopathology of experimental blood-stage malaria

Considered: A completed mid-term review form.

Interviewed:

Discussed with • applicant:

- The Chair queried why the licence holder had stated that are likely to use less overall numbers of animals than proposed, particularly in protocols 8 and 9. It was explained that the focus of the lab has evolved away from being malaria, and less work on these protocols will take place. The Chair noted the published article containing a replacement technique as positive to see and a short discussion followed on publishing culture and experiences of presenting replacement techniques within scientific literature.
- The licence holder queried the need for attending and presenting in person; the Chair explained the importance of mid-term review generally and particularly when procedures involving higher thresholds of severity are included in a licence. The Chair and emphasised the added value for AWERB provided by in person discussion with licensees as it allows AWERB to learn from their experiences as well as be updated on progress. The Chair acknowledged the additional workload involved and committed to taking this feedback into the forthcoming review of AWERB practice. The committee thanked the licensee and re-emphasised the value AWERB placed on their attending.

Outcome: AWERB supported continued work on this licence.

In subsequent discussion of the need for in person presentation AWERB acknowledged the time burden this placed on researchers but re-affirmed the value of the process for members. emphasized the importance of AWERB's oversight of severe licences in particular and the value of midterm in person updates in enabling AWERB to meet this expectation.

## 4. Report on licences processed from 31/10/2024 to 22/11/2024

The following amendments were approved by the executive committee.

## 4.1. Amendments to Project Licences

, Understanding the Role of Systemic Inflammation in
Cardiovascular Disease
, Nanotechnologies for Cancer Treatment, Diagnosis 8
Monitoring
, Vascular Calcification in Kidney Dysfunction
, Zebrafish Models to Investigate Disease Processes Associated
With Brain Haemorrhage
, Immune & Inflammatory Mechanisms in Cerebrovascular
Disease
New Therapeutics for Inflammatory Bowel Conditions
, Understanding Vision & Developing Therapies for
Blindness

A discussion took place on if researchers that submit multiple amendments on a licence have not properly considered the licence when drafting it. It was noted that a licence is usually granted for 5 years, which is a long time, and during that period the research may evolve leading to changes in the work and the need for amendments. The number of amendments in this case does not mean that the original licence was not properly planned.

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

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

prospective studies should be included in licences to account for any delay.

ASRU have revised what they class as complex licences. Legally, reviews of licences need to happen within 40 working days, but complex licences have an additional 15 working days.
 will keep AWERB updated on this so that a discussion can take place on if AWERB advice to researchers needs to be revised to ensure licences are submitted earlier or if

### 6. Standard Conditions 18s and non-compliances

- The committee were provided with a table of reports submitted to ASRU along with the reports for each incident.
- A narrative account was also provided and will be included in future reports.
- The submission of this report was later than usual due to a change in scheduling of the agenda items on rotation. It may therefore appear that there are more submissions than on previous occasions.
- The Chair thanked for the narrative account and enquired how SC18s and non-compliances are tracked. explained his system and that he has begun to create graphical representations of the data which are submitted to the Establishment Assurance Group (EAG), Chaired by the Establishment Licence Holder, who had suggested if this information should be shared with the research community. Consideration needs to be given about data protection.

### 7. Category C application for frog nerves

• AWERB recapped the previous discussions on the concerns around the proposed euthanasia method (concussion) in a Category C application to isolate the intact sciatic nerve and

- gastrocnemius (calf) muscle from frogs, which 2nd year undergraduate students dissect as part of the Physiology Research Skills Module.
- The Chair updated AWERB on the steps that had been taken with the teaching staff, including being invited to an AWERB meeting to talk through the concerns and questions.
- Further information on a simulation that other institutions use was asked to be provided to AWERB at a future date.
- Discussions took place on asking the students if they would be happy with a simulation, explaining to them that the frogs need to be bought in specifically to be killed for this practical. AWERB are unsure what students are aware of for this practical but emphasised the expectation that informed consent is important and that the practical offered opportunity to engage student learning in the wider ethical and societal challenges of animal dependent research
- The need for practical classes was raised and acknowledged, but the point was made that
  this needs to be balanced against the culture of care for animals and the staff looking after
  the animals.

**Outcome:** The Category C application was supported on the provision of substituting a Schedule 1 anaesthetic based technique in place of concussion.

The following information was provided to the applicant:

The application was considered by the full AWERB committee on the 12<sup>th</sup> December 2024. In discussion, AWERB identified four principal areas of concern:

- 1. The proposed euthanasia technique of concussion ('stunning') requires a high skillset that is possessed by only a small number of technicians. Currently, the only remaining need for this technique to be used is for purpose of BIOL20942. Consequently, it is only practiced annually. This significantly heightens the risk that it may not be performed as intended and through no fault of the technician have detrimental impact on animal welfare.
- 2. Due to the infrequency of using the technique, along with the high level of manual skill required by the method itself, the technicians involved are placed under considerable stress in the weeks preceding, and on the day of conducting, euthanasia. This has implications for personal wellbeing and the wider 'culture of care' in the facility. This was not noted in the risk assessment submitted with the Category C request.
- 3. There are some concerns as to the ethics of sourcing animals purely for this purpose and whether or not students are provided with the opportunity to give informed consent. AWERB appreciated the efforts made to avoid sourcing animals purely for this purpose. However, AWERB also noted that it may not always possible to obtain suitable animals from existent sources.
- 4. It was unclear as to whether the continued use of animals for this purpose was entirely compliant with UoM policy (clause 5.5).

After considerable discussion, AWERB was unable to support continued use of the proposed euthanasia technique (concussion) for this purpose and requests that an alternative technique be substituted. Based on best available knowledge, the alternative euthanasia technique should utilise a form anaesthetic judged most likely to be compatible with the learning objectives. As you are aware, we had hoped that we could have trialled this approach prior to our deliberations but this proved not to be possible due the required member of teaching staff being unable to make time to do so. Substituting an anaesthetic based euthanasia technique for physical concussion mitigates concerns 1 and 2 described above.

We understand that for 2024-5 there are surplus animals available on this basis AWERB was reassured on concern 3. However, it is currently unlikely that surplus animals will be available next academic year (based on current projections). If this proves to be correct animals would have to be sourced at cost and AWERB would wish to see full justification for this need if further Category C requests are made in the future. AWERB also strongly recommends students be given an opportunity to provide informed consent on the sourcing and use of animal materials for this practical. We also recommend efforts be made to integrate ethical considerations into learning objectives in line with QAA Biomedical Science and Biomedical Sciences Subject Benchmarking expectations (Human/Medical Physiology).

During discussion, AWERB noted that the University of Manchester's Policy on the use of Animals in Research and Teaching clause 5.5 established that "Animals must only be used in teaching activities where the learning objectives cannot be achieved without the use of animals or their tissues." It was unclear whether all students had opportunity to practice the manual skills of dissection that appear to justify the need for animal materials. AWERB noted that alternatives to the use of animal materials exist (e.g. simulations) and most leading institutions appear to have adopted them with no detriment to student experience (and in some cases in response to student feedback). We were unable to identify any other institution that still used this practical. If future applications are made, AWERB would ask that a thorough examination of whether learning objectives can be achieved without use of animal materials is undertaken. AWERB would wish to see a rationale with evidence to enable them to fully understand the need and be assured the proposed use complies with policy. AWERB also noted that this the above concerns are longstanding and that previous requests have been made to consider the continued necessity of using the frog nerve-muscle preparation. We again encourage that the need for this practical be considered against the learning objectives. If it is to be retained then we ask that careful consideration be given to mitigating in full the concerns articulated above.

For 2024-5, AWERB agreed to support this application on the provision that the physical concussion technique for euthanasia be substituted for a Schedule 1 anaesthetic based technique. The specific anaesthetic technique should be one that NACWOs and technicians are comfortable with implementing, does not risk detrimental animal welfare consequences, and is judged most likely to meet the learning objectives (based on the available evidence).

## 8. Understanding Animal Research

The university has received the Understanding Animal Research (UAR) Award for Openness 2024, recognising the institution's commitment to transparency in animal research. A key event contributing to this award was the "Culture of Care or Culture of Concern: Let's Debate Animal Research" held at Whitworth Hall which was organised by and the University's Communications Lead for Animal Research.

The Chair expressed congratulations on the website, and the ongoing commitment to communication and transparency.

## 9. RSCPA lay members meeting December 2024

The Chair attended the meeting and encourages members to look at the slides from the event which are on SharePoint:

Similar to recent meetings elsewhere, there was strong emphasis on CPD which AWERB will be responding to this year.

## 11. Away day 21 January 2025

The away day dates for the rest of the academic year have been set. Any topics people want on the agenda should be sent to the Secretary.

# the Chair thanked for his time on AWERB and wished him well in his new venture. It is taking a secondment from the university to spend 40% of his time at the expressed his enjoyment for being on the committee and its importance, along with praising for his work on openness in animal research. 13. NVS leaving

The Chair thanked the current NVS for all her hard work and contributions to AWERB. The NVS, who is moving back to stated it had been a pleasure working with the AWERB and animal unit.

The next meeting will be on 30 January 2025 at 10am-12.30pm.

## Dates of meetings for the 2024/2025 academic year are:

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

29 January 2026

26 February 2026

26 March 2026

30 April 2026

28 May 2026

25 June 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