ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 24 April 2025

Present: [redacted]

Apologies: [redacted]

In attendance: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 27 March 2025 were approved.

2. **Applications for New Project Licences**

2.1. [redacted], Extracellular Matrix Mediated Control of Immune Cell Recruitment & Positioning in Health & Disease

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

Interviewed: [redacted]

Committee discussion:

- The Chair discussed with AWERB which pre-submitted comments could be addressed in the feedback letter with the applicant and which members wanted to raise during the meeting.
- The Chair asked if members were comfortable with the level of detail in the NTS given the nature of some of the protocols. AWERB discussed the balance between being transparent and any concerns that may be raised regarding the contents, with an agreement that the contents of the NTS should remain as they are subject to the revisions required by the committee.
- Members wanted to clarify the Humane End Points with the applicant.

Discussed with applicant:

- The applicant was asked to explain how peritoneal irritation identified in a mouse and if it is clear what would constitute as the Humane End Point states "In the unlikely event that temporary peritoneal irritation persists for longer than 2hrs, animals will be humanely culled." The applicant explained that the animals would display with physical signs of discomfort in that area.
- AWERB asked if there are situations where a cranial window would be placed but no imaging take place, with the applicant explaining that this allows for them to look at the effect of the window itself on the surrounding tissue.
- The commitment of the researcher to making data widely available was exemplary including providing 'neutral' 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.

- The title is very technical and not easy to understand for the non-expert. Could the aim of the project be expressed in non-technical language and used as the title as this would help people to approach the NTS which will be a public document. I realise it will be tricky but something like this may work:
  - Investigating how factors outside the cell ('the extracellular matrix') control immune responses.
- As raised by the NVS in the meeting, the stated percentage of weight loss (20%) for a moderate protocol requires justification as 20% could be indicative of a severe protocol. If 20% weight loss is needed in order for your experiment to produce the required data then AWERB would support this, but we require you to look at data from your previous work and determine if the higher weight loss is needed and if so provide suitable justification. Please consult with the Compliance and Licensing Manager who will assess any justification you submit for the higher weight loss, where appropriate seeking input from the NVS/NACWO.
- Page 31 - Are repeated air pouch injections into the same site experimentally necessary (it can only be made in one place?)?

- Page 33 - Step 1: transgene induction. The way this is written does not seem to allow tamoxifen to be administered by injection (states only gavage or diet). Later there is mention of peritoneal irritation from tamoxifen, and also "where possible Tamoxifen will be administered by a single intraperitoneal injection or application to the skin" which is different from the transgene induction section - needs making consistent and clear what the intended routes of administration will be. This section will also need checking in other protocols (e.g. p49,66).
- Page 33 - What determines when you can use less invasive/stressful methods other than oral gavage/injections? Could you you briefly clarify when, for example, syringe feeding would be less efficient than oral gavage?
- Page 35 – as discussed in the meeting, it may be beneficial to include details of how peritoneal irritation is identified in a mouse. The HEP states "In the unlikely event that temporary peritoneal irritation persists for longer than 2hrs, animals will be humanely culled."
- Page 50 - Is the weight of the headplate factored in when considering the animal's weight loss as an HEP? Is the weight taken straight after surgery and this used to measure weight loss, or a different method?
- Page 54 – Please check if the first step allows you to take blood, as a reviewer queried where are the immune cells you are injecting coming from, e.g. other mice culled under S1 – or does this need to be added as a separate step in this protocol (3) and protocol 4?
- Some comments were made regarding your Non-Technical Summary which are listed below, however AWERB felt that it was a very clear NTS overall. Please update your NTS based on the comments and send it to the following lay members for their review ([redacted])
    - The NTS starts off talking about immunity to infection and the importance of glycocaylx in this process and in inflammation also. But no infection models are proposed to be studied. It's not a problem but I expected to read something about infection?
    - Perhaps explain what a craniotomy is to the lay reader - something like: surgical procedure where a section of the skull is removed? The lay reader might struggle to understand what 'Immune cell recruitment' means so perhaps a short sentence explaining that it is the process by which immune cells are attracted to sites of inflammation (if that is correct!) would be helpful on first mention. Perhaps explain to the lay reader what labelling means - is it 'attaching detectable fluorescent markers'? It would be helpful to the lay reader to have the words endothelium and reagents explained. Additionally, I'm not sure the lay reader will understand what a 'vessel cell' is. Perhaps use: cells that line the interior surfaces of blood vessels? It also might be helpful to explain that surgical implantation of a cranial window is the only way to directly image the glycocalyx and immune cell recruitment in the replacement section. Also in the replacement section, it would be great to add that the information you acquire on the glycocalyx and leukocyte recruitment will be used to inform development of in

vitro/organoid models - and I'd be very keen to eventually use anything on organoid models as a case study in the 3Rs section of the externally facing animal research website.

- Page 3-4 - The answer to 'who or what will benefit' may need just one more sentence to clarify what is meant. The information there is great - clear and succinct - but something is missing to fully follow your meaning. It may be that you introduce the 'chemokine' system and explain that we have no drugs to target it which has impact on patient health for various diseases. However you leave it implicit why this is relevant - are you implying that knowledge from this project will in the mid or long term lead to new drugs to target the chemokine system? Something needs adding in the first paragraph to make the point explicit. You could also make more explicit that researchers will benefit from the knowledge, clinicians from new diagnostic tool and new therapies, and patients will benefit from the same?
- Page 4 - Will the air pouch ever require analgesia after the post operative period, i.e. does it ever cause general discomfort or pain? How does a mouse tolerate the injection of inflammatory stimuli into it? Are they still able to be housed in groups? It would be helpful to explain in the NTS the air pouch is created on the animal's back.
- Page 4 - outreach is quite a dated term - engagement is more current - outreach presumes a linear model of disseminating information to the passive public. People learn more when engaged to think themselves. Engagement is also two way - implying research will gain something from the public.
- Page 4 – “Explain why you are using...” - perhaps a line on why you are using / need genetically altered animals would be beneficial here.
- Page 4-5 - the answer to "Typically, what will be done to an animal used in your project?" is possibly too detailed for the NTS and contains a number of technical terms (e.g. craniotomy, NVS, LPS). However it does read clearly if the technical terms were explained or simplified to non-technical language it may work.
- Page 5 - "will be assessed and alleviated where possible" - I wonder if adding managed here may avoid a misreading. The present wording suggests assessment and if nothing can be done then nothing is done. However, what would happen in practice is presumably the pain would be "carefully managed, regularly assessed and alleviated as far as possible".
- Page 5 - "but the animals will recover quickly" - perhaps better "but animals generally recover quickly" as the future is always unknown
- Page 7 - "worked with a statistician and used" - remove ‘and used’ as it is repeated later in the sentence.
- Page 8 - Typo: ... glycocalyx from tissue from animals which have been humanely killed.
- Page 9 – please revised ‘refined handling techniques’ to ‘most up to date’ as discussed in the meeting. Refined in the context

of a Project Licence has certain connotations and you explained in the meeting you mean the current best practice for handling.
- Page 12 – consider a synonym for ad-hoc.
- [redacted]

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.

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

3.1. [redacted], Understanding gene function in cardiovascular disease

Considered: A completed mid-term review form.

Interviewed: [redacted]

Discussed with licence holder:
- The implementation of the 3Rs on this licence is impressive, including limiting the number of procedures and doing surgeries in the morning. The Chair asked if these refinements are shared. The licence holder explained that anyone they speak to about their work is informed of the refinements they have made during the licence as well as the steps they have taken with regards to replacement and reduction. The licence holder felt that many of the 3Rs arose from discussions with the animal facility staff and would therefore be available to others working in the unit.
- The Chair asked if the switch to using both sexes had been met with resistance or challenges for the licence holder in their field, who explained that there was actually a push from the field itself and journals to use both sexes and in not to do so now needs justifying. Many interesting results are being seen now that both sexes are being used, including differences and similarities.
- The NVS asked how the licence holder had mitigated the potential response from people who may say a higher number of animals are being used when research uses both sexes. The licence holder and statistician discussed the need for appropriate experiment designs so that double the number of animals is not needed just because you are being both sexes.

Outcome: AWERB support continued work on this licence.

4. Report on licences processed from 12/03/2025 to 08/04/2025

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], How Immune Responses Regulate Metastasis & The Evaluation of Immunotherapies

[redacted], Understanding the Mechanisms & Pathophysiology of Heart Failure & Atrial Fibrillation

4.2. Applications for Category B work

[redacted], Molecular Control of Organ Regeneration

A discussion took place on the Category B application. The Chair noted that the application makes a mention of an IACUC approval letter, but this was not attached. The Compliance and Licensing Manager noted that the Category B/C Sub-group took the applicants on their word that they have IACUC approval because the facility is AAALAC approved. The Chair noted that in future, the main committee should be assured that the sub-group have seen a copy of each approval letter.

4.3. Applications for additional availability for new or current project licences

[redacted]: Characterisation of Brain Tumours: From Biology to Druggable Markers (Primary at CRUK MI)

The Compliance and Licensing Manager informed the committee that this is a request for a licence with its primary availability at CRUK MI to use the radiation facilities housed at the Wolfson Molecular Imaging Centre (WMIC). As the majority of the procedures on the licence will be undertaken at the Paterson and not the WMIC, this request does not raise great concern.

The Chair asked how the [redacted] transports animals effectively and safely from the main facility to the WMIC. The Compliance and Licensing Manager responded that the [redacted] is attempting to access a specifically designed van with a designated member of staff responsible for transport. The transport of animals happens in a defined manner and animals are only at the WMIC facility for a defined period required to undertake the particular procedure. The animals may then be returned to the main [redacted] buildings, or the animals would be humanely killed there, depending on the nature of the study. Designated NACWOs attend the WMIC on a daily basis while animals are there and if there were any welfare concerns, an NVS would be called to review those animals.

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. The Compliance and Licensing Manager explained to the committee that main AWERB meeting slots are full until February 2026 and that he continues to receive a certain amount of surprise when explaining the timescale to first-time applicants. The Chair asked the Compliance and Licensing Manager whether the process is approaching a position where new grants would be potentially delayed because of the existing AWERB workload. The Compliance and Licensing Manager confirmed that this is not the case and all the applicants to be seen in Autumn can begin their projects on other people's licences that they are already collaborating with. The Chair noted that this should be a topic for discussion at the July Away Day.

5.3. The NVS raised concerns about an upcoming Project Licence application, which required a 4-hour pre-AWERB sub-group meeting, with changes still to be made. The Compliance

and Licensing Manager informed the committee, that it if it is returned in an unfinished manner, then it will not come through to committee on its scheduled date. The Chair requested that he and the Secretary be informed of the outcome as soon as possible, so that there can be a rescheduling of applicants or other agenda items, if possible.

6. Estates update

6.1. The Compliance and Licensing Manager informed the committee that communications with estates and the [redacted] are improved. Any concerns are now being elevated to the appropriate level and there is a quicker turnaround in response time.

6.2. The Compliance and Licensing Manager also informed the committee that in the next couple of months [redacted] are planning a preparedness exercise, regarding an Estates failure and how the [redacted] will mitigate that. The Chair noted that it might be helpful to have an AWERB committee member as observer to the simulation exercise and volunteered to do this on behalf of the committee, if this was acceptable to the [redacted]

6.3. The Chair noted that the Estates update should remain a standing item on the agenda for now.

7. NVS report

7.1. The Chair complimented the NVS on the clarity of her new style of report.

7.2. The NVS noted that there are two reports – one dated 14 February 2025 and one dated 1 April 2025 for Q1, as she began her role as NVS part way through the last quarter. She added that as her report for the Establishment Assurance Group (EAG) and AWERB falls quarterly the report will suffice for both. The Chair highlighted to the NVS that the EAG and AWERB rotation may not fall within the same month next academic year.

7.3. The NVS informed the committee that the health surveillance and monitoring programme is in the process of being refined to suit the different facilities but is currently fit for purpose.

7.4. The NVS commended the aquatics team for their efforts during the installation of the first of two new Xenopus tank systems. This has never been done before with Xenopus laevis in place, that require movement to the new system. One animal was lost due to stressed red leg, but this was not unexpected for a tank that is known to be a little immune compromised. The Xenopus tropicalis are due to be moved on Monday 28th April. There are fewer animals, but they are known to be more sensitive. [redacted], a specialist aquatics NVS from [redacted] will be on site on Wednesday and Thursday to assist with monitoring the animals. The Chair noted that prior to the Away Day, the committee were not aware of this as an issue, but hopefully the new format of the NVS reports will mean that the committee is made aware of more ongoing activities of the [redacted] The NVS clarified that the old system was still functioning, but the BioCarb automated was not. This meant that temperatures had to be taken manually and BioCarb added by hand. The automation of the new system is much less labour intensive for the [redacted] staff.

7.5. There NVS reported that was no detectable re-occurring welfare issue seen across the SC18s submitted.

7.6. The NVS noted that her report discusses a continued concern over the lack of appropriate wild rodent control across the facilities. However, she highlighted that [redacted] is now in place for all [redacted]-owned rooms and there have been no new rodents sighted during the day. Members of the committee raised concerns about whether mice have been trapped and whether this causes biohazard issues for the mice facilities. The NVS clarified that there have only been mice sightings in the frog facility at the [redacted]

[redacted]. No wild rodents have entered the main [redacted] building where facility rodents are kept. The Chair questioned whether the true results of this mitigation effort would not be seen given the increasing temperatures. The NVS confirmed that the facility would have to wait until winter to compare.

7.7. The NVS highlighted that there is continued concern regarding the resilience of facility equipment (air handling units and autoclave) which may pose a risk to biosecurity and animal welfare. However, it does appear that estates and the [redacted] are working together to actively address these issues. The Director of the [redacted] is working to secure a second autoclave as it is currently a single point of failure. The Chair asked to be kept updated with the issue, and queries whether recent viral outbreaks were due to autoclave failures. The NVS responded that in this instance, it was not the case, but if the autoclave breaks when a viral outbreak occurs, it will have much greater consequences than the most recent outbreak. The Chair thanked the NVS for her input in finding new single points of risk.

7.8. The NVS raised concerns with the of pre-existing health issues in sheep brought into the facility having a potential impact on animal welfare and research data. She noted that she is trying to organise a meeting concerning 'large animals' for early summer and in the meantime is actively pursuing what the facility can do in the meantime to enable best practice for large animals within the facility. The NVS highlighted to the committee that this is an AAALAC requirement and as a large animal specialist, the large animal facility needs to come into line with the rest of the conscientious work taking place in the [redacted]

8. 3Rs AWERB subgroup report

8.1. The 3Rs Manager noted that the 3Rs sub-group met in March, welcoming quite a few new members, enabling the group to have a wider spread of species experience. This quarter, the group only considered retrospective reviews. There were a number of interesting 3Rs mentioned including organoid models.

8.2. The 3Rs Manager highlighted that one project licence holder raised the difficulties with getting zebrafish recognised as an acceptable model within their field of work. The Chair noted that points of resistance when changing models has come from the same licence holder before and invited the committee to share their thoughts on this. The committee concluded that the issue appeared to be field specific and suggested that perhaps Zebrafish models are more widely accepted in the developmental field and less in clinical work.

9. Any other business

9.1. Minor Administrative Amendments – Use of Teams

The meeting in May will take place over Teams. The Chair explained that it will be desirable if AWERB did not have to justify why our meetings take place over Zoom, as the rest of the University moves to Teams, and we want to re-examine the functionality of Teams for our purposes.

The Secretary informed the committee that she will be turning off the chat function to avoid a viewable record of comments, but if this causes issues for anyone, they should let either her or the Chair know.

The next meeting will be on 29 May 2025 at 10am-12.30pm.

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