MANCHESTER 1824
The University of Manchester

ANIMAL WELFARE AND ETHICAL REVIEW BODY

Minutes of the meeting held on 25 April 2024

Present: [redacted]

Apologies: [redacted]

1. **Minutes**

Agreed: That the minutes of the meeting held on 21 March 2024 were approved.

2. **Applications for New Project Licences**

2.1. [redacted], Inhibition of miRNA-29 to Improve Adhesion in the Skin

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

Interviewed: [redacted]

Committee discussion:

- The Chair asked if the application had come through to committee prematurely given there was a section missing on stats and the NTS was far too technical. The Compliance and Licensing Manager said that it had come through in good time.

- The Named Persons commented that the missing section had been seen by them so the applicant must have ticked/unticked something that meant the section became hidden.
- The process for reviewing NTSs should be discussed at an upcoming 'away day'.

Discussed with applicant:

- The revisions will need to be reviewed by all of AWERB given they have not been able to review the experimental design or power calculations.

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 32 - 'Will your experimental design be determined by a regulatory guideline?' this should have been 'no' and questions on stats and experimental design would have appeared. Given that this section is missing the revised application will need to be recirculated to the full committee.
- There are some typographical errors in the application which require correction before submission.
- Title- "Inhibition of miRNA-29 to improve adhesion in the skin" contains technical language and is not meaningful to the lay reader. Could the broad aim of the project be conveyed in the title in language suitable for a non-expert reader?
- Page 26 - " Wounds will be closed within 14 days and collected before that" What does this mean? is it a typo?
- Page 29 - Why is body weight compared to age matched controls rather than pre-surgery weights of the same animal? Same throughout
- Page 37 - Advise to include the scoring system in the PPL as this is the basis of humane endpoints.
- Page 37 - "All animals displaying blisters on ears and footpads, footpads, and tails, collectively scoring 6 will be culled using Schedule 1." - does an animal have to score 6 on all of these areas to reach the HEP, or just one body area? Clarification needed.
- Page 40 - Total sum of the score is 7. For clarity please state that the HEP is a score of 6 or above.
- Protocol 2 - Mice will be subjected to anaesthesia and analgesia - what is the schedule of analgesia?
- Protocol 2 - In the protocol details, it states that wounds will be closed within 14 days and collected before that. Does this mean that all wounds will naturally "heal" within 14 days, or that animals will be culled by day 14? Later on it says in Step 3, mice may be imaged for up to 21 days post wounding, should this be 14 days?
- Protocol 2 - 2 wounds will be created per animal and treated as independent units. Can more explanation be given here? Will one wound serve as a control? E.g. no oligo versus topical oligo? How confident are you that the treatment won't influence healing of the control wound.
- What time of day will the wounds be inflicted? Will this be standardised? Please include details in the application.

- A number of comments were made regarding your Non-Technical Summary which are listed below. However, given the number of comments the committee felt it would be more efficient if you contact one of the lay members directly who is happy to work with you on the NTS. It may be that the parts of the licence that make up the NTS need to be considerably rewritten. Please contact [redacted] for help with the NTS.
    - Can you explain what the conditions are for an extended period of individual housing following the incision of two wounds in protocol 2? Could that period of 6 days be any longer?
    - Can you explain if you are using both female and male animals in this study and if you intend to publish negative results?
    - I felt that it would be helpful for the refinement section to contain some more details around the giving of analgesia and the use of punch biopsies. And also the harms section might detail how blistering may develop on tails, ears, and footpads on some of the mice.
    - I felt the NTS would be easier for the lay reader to understand if the phrases 'wound matrix' and 'extracellular matrix' had a slightly more detailed definition as in some instances, 'Wound Matrix' appears to refer to a body process and in others an artificial scaffold.
    - Page 2 - Suggest minor editing to remove typos and improve clarity: Skin can be injured by a range of actions such as surgical intervention or unintentional trauma. Studies in mice have already shown that small wounds on their backs heal very efficiently when filled with wound matrix, (Is this a type of artificial scaffold ?) designed to promote wound healing and tissue regeneration. The aim of this project is to find out how wound matrix functions. Furthermore, the identification of adhesive molecules that improve the formation of wound matrix could help wound healing and alleviate disorders such as epidermolysis bullosa (EB), which is characterized by fragile skin that blisters and tears easily.
    - Page 3 - line 1 - the inclusion of 'also' does not seem to be necessary - wording such as "Skin acts to protect the body and in this role is often damaged" might be clearer?
    - Page 3 - "how adhesion works" is adhesion a technical word for a stage of healing? Could you say healing? Or is not could you define in lay language what adhesion is/means?
    - Page 3 - " more efficient skin repair and healing of ulcerated (e.g., diabetic) wounds" - this type of language is far more lay friendly and meaningful to the non-expert
    - Page 3 - " the development of wound matrix assays" - perhaps explicitly state "with potential applications for the replacement animals"?
    - Page 3 - "Patients with EB may eventually benefit as well from the development of the treatment" - is human benefit and new treatments a separate 4th category? I wasn't clear how it related to animal welfare?

- Page 3 - I'm not sure the general reader will understand what an Oligonucleotide is. Can you explain it in lay terms? is it something like: molecules artificially synthesized in the laboratory used in various applications in molecular biology? What is the difference between an Oligonucleotide and a wound matrix? is it the same thing?
- Page 3 - Can we say instead of wound matrix assay, experimental methods to evaluate the effectiveness of wound healing or tissue regeneration treatments using wound matrices? And can you explain what microRNA-29 is and why it is important to this study?
- Page 4 - Suggest this: Genetically modifiable and genetically controlled breeding lines make it possible to test specific molecular mechanisms by turning different genes on and off.
- Page 4 - Suggest: Mice will be bred to achieve the genetic type needed for experiments by deletion of specific genes.
- Page 4 - Suggest: Wounds will be treated with a simple dressing pre-soaked with oligonucleotides. If the dressing doesn't stay on, the oligonucleotides will be injected near the wound site once, after wounding has been administered.
- Page 4 - Suggest: All animals are expected to make a rapid recovery from the anaesthetic within two hours. Animals that fail to do so or exhibit signs of pain, distress or of significant ill health, which is rare, will be humanely killed.
- Page 4 - Not sure I understand this sentence: For the EB blistering model, mice will be breeding to another genetically modified line to rescue the blistering disease genetically. Perhaps for rescue you could say 'heal' or 'start the healing process'?
- Page 4 - is there a difference between pain killers and anaesthetics?
- Page 4 - Under what will be done to the animals, in terms of the EB models, It's not clear to me what exactly the mice will experience, how long they will experience it for, and how it will be mitigated.
- Page 6 - I wasn't clear from the text if the group is looking to develop a human in vitro model of wounds modifiable by the oligonucleotides as a total replacement?
- Page 6 - Suggest: In microRNA-29 knock-out experiments, the control mice will be wild-type (wt) littermates. They will be compared to another group of mice that receive oligonucleotides applied to one of two wounds. Doing this helps us make better comparisons between the mice and get clearer results from the experiments.
- Page 6 - "By reading the scientific literature, I will avoid repeating anything that has already been done" - I take the point but do we need to say this?
- Page 7 - Not sure I fully understand: My group is also using computer modelling to analyse wounds, receives, and shares wound blocks for sectioning and imaging with other groups. Can you explain wound blocks?

- Page 7 - Can you explain what junctional epidermolysis bullosa is? Perhaps this might be appropriate?: The Junctional Epidermolysis Bullosa mouse model (JEB) we're using, where outer and inner layers of skin are separated, has less severe symptoms compared to both other mouse models and the actual disease in humans. It is the most suitable model for the specific purpose of the study which allows us to focus on the specific genetic mechanisms involved in the condition and potential treatments, despite the mouse model not fully replicating the severity seen in human cases of JEB.
- Page 7 - Perhaps this would suffice: Unlike mammals, lower organisms commonly used in tissue regeneration studies such as the fruit fly lack microRNA-29.
- Page 7 - "The animal facility at the Establishment regularly conducts workshops on 3R, and this information is updated on the Establishment SharePoint" - minor point but this is a statement that does not quite explain how YOU will stay informed. Perhaps add a word or two to indicate you will attend, and regularly engage with, these resources?
- Page 8 - "How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals? " - the answer to this question is very hard to follow as a lay reader due to the technical language. It also appears (though I may be misunderstanding) to be referring to methods of reduction and replacement (use of fewer animals) as opposed to clearly stating the refinement steps to minimize welfare cost / harm to animals subject to procedures?
- Page 8 - "What published best practice guidance will you follow to ensure experiments are conducted in the most refined way? " - is it possible to provide a clear statement on the guidelines that shape the work? There is usually reference to literature such as the ARRIVE guidelines, and/or guidance issued by NC3Rs and LASA. Or support by NVS. Are there specific guidelines for skin wound research such as this that could be referenced?

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

3. Applications for Amendments to Project Licences requiring full committee review

3.1. [redacted], Immune & Inflammatory Mechanisms in Cerebrovascular Disease.

Considered: A Home Office amendment summary sheet and highlighted revised project licence.

Interviewed: [redacted]

Revisions:
- In liaison with [redacted], revise the Humane End Points for the DSS model so that it is transient weight loss of up to 30% or failure to gain weight within a certain period of time (to be discussed and agreed with the Named Persons).

- Inclusion of aged mice.
- More information on the scoring systems you will use, including for example what 'excessive' rectal bleeding will be and stool condition. This is especially important for the mice treated with DSS.
- Given the proposed changes to the licence, advice should be sought on if the aims still accurately reflect the licence, and if not, consideration should be taken on if they need to be updated, particularly for section in the NTS.

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. Report on licences processed from 06/03/2024 to 10/04/2024

The following amendments were approved by the executive committee.

4.1. Amendments to Project Licences

[redacted], Immune Regulation of Health & Disease in Mucosal Barrier Tissues

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

[redacted], Pathology & Treatment of Orphan Diseases, (Transfer Primary Availability to University of Edinburgh).

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.

6. NVS report

6.1. No comments were made in relation to the reports from February and March 2024.

7. 3Rs AWERB subgroup report

7.1. The Chair of the 3Rs AWERB subgroup highlighted that two licence holders who recently submitted reviews to the subgroup would be coming to talk to AWERB at future 'away days'.

8. Anaesthesia and euthanasia guidelines

8.1. The committee endorsed the documentation provided by the animal facility on anaesthesia and euthanasia, specifically the policy on euthanasia in laboratory animals, anaesthesia and analgesia of laboratory animals and guidance for sheep anaesthesia.

9. Construction work on 3rd floor BSF

9.1. The work has been stopped until a solution can be found that does not disturb the animals. This solution will be identified jointly with estates and the research community. The extent of the impact on welfare of animals is unknown. The facility Director is optimistic that a similar situation will not occur again, and that estates will discuss any planned works with the animal facility prior to work commencing.

10. Power/heating issues in the BSF

10.1. The Director is waiting for a report from estates about the current power issues. This will be shared with AWERB in due course.

The next meeting will be on 23 May 2024 at 10am-12.30pm.

Dates of meetings for the 2023/2024 academic year are:
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
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18 December 2025