



- The applicant explained about the use of different diets for wild type versus genetically modified mice.
- The need for pilot experiments was discussed by the committee and made a requirement for supporting this application.

*Revisions:*

- The Committee agreed that pilot work should be carried out for the protocols involving fasting and the results of the experiments discussed with the BSF before any further work can be carried out.
- When discussing weight loss, the humane end point should be if weight loss reaches 20%, not greater than 20% weight loss.
- The period of fasting needs to be consistent throughout the licence.
- The timing of fasting needs to be clarified in the licence for the experiment involving constant darkness.
- Please check that the numbers of animals listed in the licence and the AWERB form match and are the most up to date.
- A scoring document needs to be included in the application for Protocol 2 rather than referencing the paper, Smith et al. 2018. Specific humane end points should be outlined.
- The committee noted that in your presentation you said you were going to use both sexes but in your application you only mention using male mice. If you want to look at how methylation affects sex this should be included in the application.
- On page 33 and 45 of your draft project licence, you discuss the use of Biolumicorder cages. Please clarify if mice will be given Luciferin in drinking water? If so, you may need to add permission to alter drinking water and consideration of making it palatable to prevent dehydration to the licence. Please discuss this with the BSF.
- Please clarify the age of the adult mice that you will be using. Will these be over 8 weeks old?
- In response to the question "Please explain if you will publish negative findings and make the raw data open access?", you state "Yes, any scientifically robust results will be published, and data made available in repositories as appropriate." Please provide information on which repositories you use for work of this nature.
- On page 7 of 70 there is a typographical error for methyl donor (not donour)
- On page 19 of 70 you mention duplication of work. Please expand on the justification for this.
- Please check that any abbreviations are explained of their first use, e.g. p33 of 70 mentions CLAMS, TSE cages and LESA Biolumicorder.
- 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]  
[REDACTED]  
[REDACTED]  
[REDACTED])
  - NTS p4 - "gavage" is used without explanation
  - NTS p5 (& in other places), Fate of animals: please use "humanely killed".

- NTS p7 - “expressing a luciferase reporter” is used without explanation
- NTS p7 (Refinement). I don’t think the author means “nefarious” which = wicked/criminal
- If you are using enrichment for animals in single housing please include this 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 and on the basis that pilot experiments are conducted and the results discussed with the BSF.

**2.2. [REDACTED], Models of Tissue Injury, Regenerative Repair and Reconstruction in the Limb & Appendages**

*Considered:* A completed AWERB form and PPL application

*Interviewed:* [REDACTED]

- Revisions:*
- Please discuss with the BSF the need for anaesthesia. Usually IV injections are done without anaesthesia.
  - Please clarify the wound size. The size of the injury seems to be too large (page 10 of 95). If the cut is transverse then 6 mm would appear to encompass the digit of a mouse.
  - On Page 29, please include specific ways you will monitor animals following chemoablative therapy and injection of bone marrow, e.g. posture, failure to thrive, etc.
  - On Page 29, please include adverse side effects associated with repeated injections when given every day for 5 days. Clarification on if you are targeting the same spot should be included.
  - On page 31, there are comments about work under terminal anaesthesia. Are these relevant to optional step 2 which is about blood smears? Please provide clarification.
  - Page 39 and 41, please provide specific details on what ‘Vigilant monitoring for pain and distress’ will encompass – e.g. hourly/daily/weekly?
  - Page 52, please clarify if there are any refinements for the mouse? Protocol 2 is just mice and 3 is mice and rats yet in the question on refinement the answer states that no refinements have yet been developed for mouse.
  - Please reword the section in Protocol 2 which states that ‘up to 5% (up to 20) or 5-10% (20-40) are expected to die’. If you expect no more than 5% then this is what should be included.
  - Please check the document for typographical errors, including on p12, para 3 - biofarbicated for biofabricated ?
  - On page 51, units need to be included in the table.
  - 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]

[REDACTED]  
 [REDACTED]  
 [REDACTED])

- NTS - could be made more concise to aid reading for the lay person. For example, the sentences "The injury types will be simplified from those seen in the clinical setting. We will also aim to use enhanced healing methods to create new tissues for healing or replacement organs." under aim of project did not seem to be necessary to communicate the key point.
- The benefits section would be better if it were more definitive.
- P3 of 8, Who or what will benefit - 1st paragraph - Last sentence : Presumably would be ' We would AIM to have...'
- In the refinement section please include the use of sterile equipment.
- Perhaps part of your active work to develop replacements to animals involves action to keep up with literature on the 3Rs? It is great that the BSF keeps you updated but it would be good to convey that active steps you and your team take to keep up with innovations; mention the passive reception of information by all means but stress the action you take. Ideally, rather than simply saying you are developing systems could you provide a concise sentence on the actual work being done?
- NTS p3 - Missing word? hope to have
- NTS p5 (& in other places) Fate of animals: please use "humanely killed".
- NTS p6 - "vascular tissue engineering model (AV loop)" – unclear for the NTS
- NTS p7 - Missing material – paragraph ends in mid-air?
- On page 7 of 8 (and repeated on page 88 and 95 of 95) at the end of the section on refinement there is an omission. The text just says "If animals"

*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 and retrospective reviews requiring licence holder attendance at the meeting

#### 3.1. [REDACTED], Understanding Mechanisms of Fibrosis

*Considered:* A completed mid-term review form.

*Interviewed:* [REDACTED]

- Discussed:*
- The use of male animals only was discussed. Clinically men get fibrosis more than women, potentially due to oestrogen.
  - The licence allowed for work in rats however only mice have been used so far. As the work has progressed the researchers have identified specific factors they are interested in and for which they can only use transgenic mice for.
  - The researcher was asked if any change in nutrition was given after surgery. The animals are provided with wet mash and kept in a warming cabinet.

*Outcome:* Approval for continued work.

**3.2. [REDACTED], The role of inflammation in cerebrovascular disease**

*Considered:* A completed mid-term review form.

*Interviewed:* [REDACTED]

*Discussed:*

- The use of the MRI is a significant refinement and was discussed with the researcher.

*Outcome:* Approval for continued work.

**4. Responses from Project Licence holders regarding queries from mid-term/end-of-licence reviews (for information only)**

4.1. [REDACTED], The contribution of mast cells mediators in inflammatory skin diseases (end-of-licence review).

**5. Breeding guidelines**

A paper on the progress on the development of guidelines was provided to AWERB prior to the meeting. The guidelines will be simple and will help to build on relationships already in place between researchers and BSF staff.

**6. Retrospective review**

The comments provided to the Secretary prior to the meeting were discussed. Further comments were requested based on the comments of [REDACTED]. An updated form will be provided at a future AWERB meeting.

**7. Report on licences processed from 06/08/2020 to 17/09/2020**

The following amendments were approved by the executive committee.

**7.1. Amendments to Project Licences**

[REDACTED], Brainstem Circuits Controlling Gut-Brain Communication.  
[REDACTED], Regulation of Glomerular Barrier Function in Health & Disease.

[REDACTED], Type 2 Immunity in Infection & Maintenance of Tissue Health

[REDACTED], Fish Physiology in an Era of Climate Change

**7.2. Applications for Category B work**

[REDACTED] Age-Related Remodelling of the Sinus Node.

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

The schedule for future meetings and the status of past applications was provided to the members.

## 9. NACWO report

- Reported:*
- The Director of the BSF reported that the BSF is now operating as normal. All staff are in and adhering to social distancing. Staggered starts have been introduced to help with reducing the amount of staff in at one time, this means that the BSF now have 12 hours cover.
  - ██████████ thanked the Director of the BSF and his staff for all their work over lockdown.

## 10. NVS report

- Reported:*
- The number of weekly visits to the BSF by the NVS has increased following the increase in research activity.
  - There are no concerns regarding animal welfare.

## 11. Standard Conditions 18s

- Noted:*
- Five Standard Conditions 18s were reported since the last meeting. Discussions take place with the project licence holders to ensure the issues do not happen again.
  - The Director of the BSF was waiting for a reply from the Home Office for two of five Standard Conditions 18s.
- Reported:*
- The response time from the Home Office does vary after submission of Standard Conditions 18s. The Act does stipulate a time limit for submission of Standard Conditions 18s and a response from the Home Office. The BSF have always submitted Standard Conditions 18s within the required timeframe.

## 12. Matters arising from previous meetings not covered elsewhere on the agenda

### 12.1. Update email to applicants to explain that there are sections on the Home Office form that self-populate into the NTS and it is advised they make a note of these as they fill in the form.

██████████ has created a 'top tips' document for researchers using the Home Office system. The Secretary will circulate the document after the meeting and invites comments to be sent back to her.

### 12.2. Update adverse event document provided to applicants for project licences.

██████████ and ██████████ have updated the document

### 12.3. Mentoring system

This will be discussed at a future meeting.

### 12.4. AWERB questionnaire for researchers

A short questionnaire has been developed for researchers who have submitted project licence applications to AWERB. The draft questionnaire will be circulated after the meeting and the Secretary invites comments to be sent back to her.

### **13. NC3Rs Regional Programme Manager update**

#### **13.1. Self-assessment tool**

The NC3Rs have been working a self-assessment tool for 18 months. The tool will allow the University of Manchester to benchmark their 3Rs work. The idea is that a number of people will be asked to complete it and a score will be given, along with some real-life ideas on how 3Rs activities can be improved

#### **13.2. Non-mammalian models workshop**

A workshop is being organised for the three Universities that Jo works with. The workshop is planned for mid-November. Details on the workshop will be circulated at a later date.

#### **13.3. Breeding resource**

The NC3Rs have developed a resource for breeding and colony management which has a lockdown focus. Details of this can be found at the following website:

<https://nc3rs.org.uk/breeding-and-colony-management>

### **14. Any other business**

#### **14.1. 3Rs subgroup**

The Chair raised the idea of forming a 3Rs subgroup which would report to AWERB. Jo Stanley has produced draft Terms of Reference for the 3Rs subgroup which will be circulated in the papers for the next meeting, at which a discussion will take place about the remit of the 3Rs subgroup and how it will operate.

#### **14.2. Home Office Inspector**

██████████ is taking a year's sabbatical to work on a project within the Home Office. The University of Manchester will have an interim inspector for this period.

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The next meeting will be on **Wednesday** 18 November 2020 at 10am-12pm, via Zoom.

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### **Dates of meetings for the 2020/2021 academic year are:**

8 October 2020

Wednesday 18 November 2020

21 Jan 2021

4 March 2021

15 April 2021

27 May 2021

8 July 2021

19 August 2021 - no licences to be seen this meeting. AWERB processes meeting.

30 September 2021