CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

24th August 2023 (via Zoom)

### MINUTES

### Present:

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| 23/08-01 | Apologies |
| 23/08-02 | MinutesThe minutes of the meeting held on 29th June 2023 were considered by the Committee and were approved. |

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| 23/08-03 | Matters Arising23/06-07-1 *Assessing the efficacy of viral vector-mediated gene delivery to the central nervous system* has been amended and submitted to ASRU.23/06-07-2 *Mechanisms of Bacterial Cancer Therapy: Investigation of the effects of Salmonella enterica spp. on intestinal cancer suppression (amendment)* has been amended and submitted to ASRU. |
| 23/08-04 | Chairperson’s ItemsThere were no Chairperson’s items. |
| 23/08-05 | Verbal Reports from the Director of BMSU, NVS and NACWOs* One of the BMSU members of staff who was a NIO and Home Office Liaison Contact (HOLC) has left, but continuity has remained as these roles are also held by other staff within BMSU.
* The role of Assistant Director of BMSU has been advertised and will be interviewed for shortly.
* Following an Institute of Animal Technology Midlands Branch event an animal technician from another Establishment has visited BMSU for the sharing of best practice.
* A chick embryo facility is being set up within the university. This facility will use embryos that are killed prior to being included under ASPA, but to ensure considerate and ethical use of the embryos, researchers working with them will undertake the Ethics and Law Modules of the PIL training programme. The chick embryo facility will be within a secured room, and AWERB should be reassured that standard operating procedures will be shared with BMSU to ensure appropriate management processes are in place to ensure compliance. BMSU has been in contact with other establishments that have similar facilities to share best practice. It was suggested that once the facility is set up, with permission from the PI in charge, then other researchers should be made aware of the facility and the opportunity for partial-replacement of the use of animals in some situations.
* AWERB Committee Members were invited to visit the BMSU Facility on 11.30 on 22nd September.
* There has been a non-compliance issue involving a procedure being performed under full anaesthetic where a probe was attached to the skull rather than the skin as described in the PPL. There was no impact on animal welfare. This has been reported to the Home Office and the response has been that no further action is required.
* There has been a non-compliance issue where mice were found without food. Actions and measures have been put in place to prevent this happening again. A report has been submitted to the Home Office and an outcome is pending.
* The government are introducing new processes around the import of animals into the UK. It is still unsure what impact this will have on BMSU activities.
* Alternative methods for health screening of the aquatic species is currently under investigation, including the possibility of screening filters rather than samples from the animals themselves.
* There is some building work going on in BMSU, but disruption to the animals has been minimal so far.
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| 23/08-06 | Report from the Fast Track ProcedureAll applications are uploaded to Teams for comments and are then progressed.There were some concerns around an application to undertake surgery in pigs overseas. AWERB has requested further information in order to seek reassurance that the work will be undertaken to standards that would meet Home Office guidelines were it to be performed in the UK. Once the details have been received, it will be reconsidered. In reply to a question raised by an AWERB member, it was noted that if AWERB is not satisfied following consideration of the information requested, then it can escalate concerns to the UoB Research Ethics, Governance & Integrity Committee (RGEIC).  |
| 23/08-07-1 | Project Licence Applications1. *Understanding the role of inflammation and fibrosis in conjunctival scarring*

SummaryThe stated aim of this project is to understand how conjunctival scarring can be controlled and associated vision loss with ocular membrane pemphigoid (OcMMP) can be reduced. This project also aims to identify new anti-scarring drugs that can be used to alleviate sight loss in OcMMP.* OcMMP occurs in over 20 million people worldwide and creates chronic conjunctival inflammation, progressive scarring and debilitating symptoms of constant irritation, pain and dryness.
* Treatments involve immunosuppression, but these have little effect on scarring.
* For half of patients, scar formation continues, and 20% become irreversibly blind.

The Committee raised the following points:* It was queried whether the PI was the best person to hold the licence as the PI’s previous experience related to the back of the eye rather than front of the eye. The PI argued that although new to this area, they have experience of ophthalmology, which involves understanding the entire eye under different pathological conditions.
* The approach has already been undertaken and published in both mouse models and humans, so it was queried what this study will add. The PI explained that this study will consider the molecular pathways which underpin the disease, and once the pathways are understood, eyedrops can be developed for treatment.
* This is a model new to both the University and the PI. It was therefore queried whether there was anyone within the UK running this model with whom BMSU and the PI could liaise in order to gain better understanding of how the model progresses and to ensure appropriate adverse effects and humane endpoints. The PI explained that whilst this model is widely published, the only UK-based PI performing this model had retired. In discussion with the PI, it was agreed that a member of AWERB would contact the retired PI to ask if they are willing to share knowledge and expertise. It was also recommended that the PI applying for the PPL should contact the animal facility where the work had been undertaken to seek any knowledge or advice they may have. It was agreed that the most likely outcome is that a small pilot study would be initially undertaken to establish the model and obtain baseline in-house data. This would be a stop: go point of the PPL.
* The need to gain further guidance on the humane end points relating to this disease model was emphasised by AWERB: it was felt this could be aided by information obtained from elsewhere. A particular concern was raised over the fact that eye irritation is difficult to alleviate, that the animals may continue to scratch so making the eye swell and close. This in turn would make eye scoring difficult as there would be uncertainty on the state of the eye underneath the swelling.
* It was noted that eye pain is not discussed in the PPL application, and that details of any pain relief should be included. Importantly, it is not made clear whether pain relief drops would impact on the molecular pathways under investigation.
* It was stated in the application that less sentient animals are unsuitable due to technical reasons; it was agreed that elaboration is required on this point.
* There were several queries about the power calculations mentioned in the application. It was noted that the values used for standard deviations should be included and the effect size of 0.75 should be explained. The PI indicated that the effect size is a biological score and based on the inflammatory rate score, but AWERB were concerned that the scoring procedure lacks clarity
* It was agreed that there needs to be further discussions with individuals and establishments who are familiar with the model and who are used to looking after animals that have undergone the procedure. Further evaluation of the application cannot progress without this information.

**Decision: The Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to the application being re-submitted to AWERB for further discussion.**  |
| 23/08-07-2 | 1. *Platelets in Haemolytic Diseases (amendment)*

It was noted that this amendment had been brought to a full meeting of AWERB because it concerns a PPL classified as severe.The amendments include * changing the breeding protocol from severe to moderate, whilst recognising that Sickle cell mice are hypersensitive to touch and light, which must be taken into consideration,
* amend Protocol 3: Assessing the efficacy of long-term targeting of platelet activation to prevent progressive organ damage. Extend protocol to 9 months so that an anti-platelet drug can be added to diet for 6 months with bleeds every 2 weeks to monitor organ function and platelet inhibition.

The Committee considered the following points:* The amendment to the breeding protocol follows in-house experience of this mouse strain. The animals are developing the disease, but the adverse effects are not as pronounced as first anticipated. Hence, it is proposed that the severity can be reduced to reflect the reality.
* In relation to the proposed long-term observation of the effects of inhibiting platelet activation, it is argued that the regular blood sampling allows organ function to be monitored to both establish if the interventions are effective, and to more closely monitor disease development.
* It was explained that humans with sickle cell disease, which is genetically determined, have spontaneous painful, sickling crises whose triggers include touch, light, and also noise. As the number of painful events increase over time, it was questioned what precautions are taken to avoid all these triggers in the mice, if they are to be kept for longer. It was explained that to help reduce these triggers, the mice are handled carefully, noise is kept to a minimum, and animals are kept away from direct light sources wherever possible.
* Since this strain of mouse has not been kept in-house for this length of time previously, it was suggested that a small group of animals should commence on the study 4-5 weeks ahead of the main cohort, so as to quickly identify and remedy any potential issues before they impact a larger cohort.
* It was noted that the drug used for treatment includes some anti-inflammatory actions as well as combatting platelet activation, so it is anticipated that it will also provide some pain relief. The humane end points are in place but need to be reviewed and confirmed for this protocol and animals will be carefully monitored throughout the protocol. It is proposed that the agent will be given for a maximum of 6 months.

**Decision: The Committee approved the amendment pending the minor changes discussed and agreed it could then be submitted to ASRU.** |
| 23/08-08 | Matters relating to the 3Rs* The Midlands 3Rs symposium is on 21 September. We currently have 18 poster abstracts and around 70 people registered. There is still space for 30 more, and so further registrations will be encouraged.
* A new refined mouse handling e-learning resource is available: <https://nc3rs.org.uk/3rs-resources/refined-mouse-handling-course>
* The NC3Rs are launching four CRACK IT challenges in early September. Large sums are offered to those who apply to solve any of the challenges. These grants have recently funded researchers from universities to solve these challenges, so they are not just aimed at SMEs.
	+ Launch webinar – SensOoChip Challenge: increasing reproducibility and predictivity of organ-on-chips. Tue, Sep 5th 2023, 14:00 - 15:15. (£2.6M over 5 years)
	+ Launch webinar – CrossDART Challenge: Multi-species *in vitro* developmental toxicity testing. Wed, Sep 6th 2023, 10:00 - 11:15. (£1M)
	+ Launch webinar – FET4Thyroid Challenge: A fish eleutheroembryo test for thyroid activity. Wed, Sep 6th 2023, 14:00 - 15:15 (£100k)
	+ Launch webinar – aTRACKtive Challenge: Early-life identification system for mice. Thu, Sep 7th 2023, 14:00 - 15:15 (£100k)
* BMSU will be trialling the fish enrichment domes in the holding tanks.
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| 23/08-09 | Condition 18 ReportsThere were no Condition 18 reports. |
| 23/08-10 | Retrospective ReviewThere were no retrospective reviews. |
| 23/08-11 | Any Other Business. It was queried whether PPL holders who have a severe protocol licence should report back to AWERB 12 months after the licence is approved. This would provide the committee with an update on project progression and whether there had been any learning points or opportunities to refine the severe protocol. **This was agreed as an action going forward.** |
| 23/08-12 | Date of Next MeetingDates of future meeting:28th September 2023 via Zoom9th November 2023 via Zoom14th December 2023 in person (room tbc)25th January 2024 via Zoom7th March 2024 via Zoom18th April 2024 in person (room tbc)6th June 2024 via Zoom11th July 2024 via ZoomAll will be from 10am until 1pm. |

**GLOSSARY**

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| 3Rs | Replacement, Reduction and Refinement |
| ASPA | Animals (Scientific Procedures) Act 1986 |
| ASRU | Animals in Science Regulation Unit  |
| AWERB | Animal Welfare and Ethical Review Body |
| BMSU | Biomedical Services Unit |
| HOLC | Home Office Liaison Contact |
| NC3Rs | National Centre for the Replacement, Refinement and Reduction of Animals in Research |
| NCTO | Named Competency and Training Officer |
| NACWO | Named Animal Care and Welfare Officer |
| NIO | Named Information Officer |
| NTS | Non-Technical Summary |
| NVS | Named Veterinary Surgeon |
| OcMMP | Ocular Membrane Pemphigoid |
| PI | Principal Investigator |
| PIL | Personal licence (Procedure Individual Licence) |
| PPLs | Project licence (Procedure Project Licence) |
| UoB | University of Birmingham |