CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

28th September 2023 (via Zoom)

### MINUTES

### Present:

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| 23/09-01 | Apologies |
| 23/09-02 | MinutesThe minutes of the meeting held on 24th August 2023 were considered by the Committee and were approved. |

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| 23/09-03 | Matters Arising23/08-07-1 *Understanding the role of inflammation and fibrosis in conjunctival scarring* will be amended and returned to AWERB for further comment prior to submission.23/08-07-2 *Platelets in haemolytic diseases (amendment)* minor changes have been completed and the application has been submitted to ASRU. |
| 23/09-04 | Chairperson’s ItemsThere were no Chairperson’s items. |
| 23/09-05 | Verbal Reports from the Director of BMSU, NVS and NACWOs* Several external visitors have been hosted by BMSU resulting in the sharing of knowledge and approaches.
* The lift installation is progressing with minimal disruption. The noise disruption has not been as significant as expected, and animal welfare has not been impacted. Once the lift work has been completed, there will be a full building clean-down.
* Some building work had been required to repair a damaged pipe. Prior to this, a review was undertaken to identify any potential risks to animal welfare and any appropriate control measures that would be required; no risks were identified.
* No feedback has been obtained from the Home Office in relation to the non-compliance reported at the last meeting.
* The Director of BMSU attended the most recent HOLTIF meeting where a representative from the Home Office was in attendance. It was reported that a number of new Inspectors are joining the Home Office team on fixed term contracts.
* No feedback has yet been received regarding the Condition 18 form submitted previously. From discussions at the HOLTIF meeting, this is not itself a concern.
* The number of iterations (times that a licence is returned for comment prior to being awarded) has increased. Nationally the figure is 2.62. Birmingham has gone from 0 to around 1. The comments are normally clarification questions. Once the comments are addressed and the application re-submitted the licences are normally awarded within 48 hours. The issues of typographical and grammatical errors were discussed, and PIs are encouraged to proof-read their applications carefully prior to submission.
* Prior to the meeting, a Committee member had approached the Chair and explained that due to logistical reasons they needed to be replaced on the committee. They had suggested a suitable individual; this was considered by the committee and the individual will join AWERB from the next meeting. The outgoing member of AWERB was thanked for all their input.
* Having previously replaced the source of irradiation used in the BMSU, some experiments were not progressing according to the expected timelines. The work has been paused whilst a review is being undertaken to identify any underlying variables that may be causing the issue.
* It has been challenging maintaining a surgical plane of anaesthesia in sickle cell mice without the animals going so deep that they have to be humanely killed. It had been identified that this was likely to be for scientific reasons in that the animals are thought to be entering into a sickle crisis prior to anaesthesia, meaning that the red blood cells are unable to carry oxygen as effectively. The situation is being reviewed to establish whether this crisis can be prevented prior to anaesthesia being induced.
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| 23/09-06 | Report from the Fast Track ProcedureAll applications are uploaded to Teams for comments and are then progressed.There were some questions raised on an application to undertake collaborative work overseas that involved surgery in pigs. 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. No comments have been received from the researcher to date. |
| 23/09-07-1 | Project Licence Applications1. *The impact of inflammation on the propagation and resolution of deep vein thrombosis*

SummaryThe project aims to establish the inflammatory mechanisms that regulate development and growth of blood clots in veins, and the involvement of these mechanisms in dissolution of the clot. * Deep vein thrombosis (DVT) is a severe life-threatening disease that strikes over 60,000 people in the UK every year despite all prophylactic measures.
* Essentially, DVT is the formation of a blood clot in a vein (i.e., the blood vessels bringing the blood back to the heart). This clot causes pain and difficulty to walk, and can get dislodged and travel to the lungs. When this occurs it can occlude one of the vessels in the lung leading to compromised oxygen exchange and, potentially, death.
* DVT is the third most dangerous cardiovascular disease, with only myocardial infarction and stroke having higher mortality rates.
* Recent studies have discovered that inflammatory factors are tightly involved in the regulation of various aspects and stages of DVT development.
* Virtually all drugs currently used to prevent or treat DVT in clinical practice cause bleeding complications in a proportion of patients, which makes identification of new and safer therapeutics a very important and timely research task.

The Committee raised the following points:* The PI was asked to explain the surgical procedure in more detail. It was confirmed that this was major surgery under anaesthesia, involving exposing the vena cava through the abdomen. The vena cava is either partially or completely occluded before the abdomen is re-closed. The PI explained that bleeding risks tend to occur whilst separating the vena cava from the aorta and if bleeding cannot be controlled then the animal will be humanely killed under anaesthesia. It was explained that post-operatively the mice recover and tolerate the procedure well.
* The committee queried how reproducibility was achieved between animals. The PI confirmed that the closing of the vena cava is comparable between animals by using mice of a similar age and weight, and a 31-gauge needle as a spacer around which the ligature is tied to achieve 90% closure of the vessel.
* The application involves two models of DVT; one complete vena cava closure, and one partial vena cava closure. The need for both models was queried and whether these are both models of the human disease. It was confirmed that these model different mechanisms of the human disease and so provide different data from each other.
* The experimental plan included allowing 21 days post-procedure to study recanalisation of the occluded veins. It was queried whether this was sufficient time, but the applicant explained that this reflected the situation in the clinic where humans are reviewed 3 weeks post-event.
* There are some queries around the humane end points that need to be addressed. This included whether animals were likely to experience hind-limb paralysis as was described. The applicant clarified that based on experience, 2-3% of animals may have hind limb weakness post-recovery. However, animals will be humanely killed if they have failed to regain movement after 45 mins post-recovery from anaesthesia.
* The NTS needs to be made more lay as it is still quite technical.
* The application states that animals will be their own control, however it was not clear how. It was explained that rather than using multiple mice, measurements can be taken at intervals in the same animal over a 48-hour period, reducing animal use and reducing statistical variability.
* A resource calculation was mentioned rather than a power calculation, and there were no standard deviation figures included. This will be checked and updated.
* There was a query around blinding and randomisation. The PI confirmed that the this already being undertaking and will be included in the protocols.
* Overall, the application is well written. In addition to the points raised above, there are a few typographical errors that need to be addressed and the adverse effects in the NTS need to be expanded. There has been some fantastic replacement work as described later in the application, and this needs to be highlighted in the NTS section.

**Decision: The Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to the application being amended and submitted to ASRU.**  |
| 23/09-07-2 | 1. *Repairing the damaged brain after traumatic brain injury (amendment)*

The amendments include * Addition of sham animals for the weight drop model (Protocol 1-4). Shams will undergo all the procedure except the weight drop itself in order to determine whether the surgical event itself impacts on the data obtained.
* Removal of “single direct injection into the brain (with and without stereotaxic coordinates” (Protocols 2 and 4).
* Addition of photobiomodulation (PBM) in Protocol 2. This involves the application of red/near-infrared light for intended therapeutic benefit.
* Addition of novel object recognition test for memory performance in Protocol 5.

The Committee raised the following points:* The scientific rationale was discussed for the use of PBM. It was explained that nitric oxide and oxygen compete for the same site on the mitochondria, and it is thought that PBM decreases nitric oxide availability thus allowing the oxygen to bind to the mitochondria and so promote neurone metabolism and regeneration.
* It was confirmed that PBM does not emit a significant amount of heat so there are no welfare concerns around its use.
* The PPL holder took the opportunity to update the committee on progress more generally as the weight drop model of traumatic brain injury had been new to the university. A pilot study has been completed, and the animals recovered well from the anaesthetic. They were less playful than normal as expected, but this improves over time. The single weight drop has been piloted initially, but the licence does permit multiple weight drops to better model what happens in practice e.g., football and rugby head injuries.

**Decision: The Committee agreed that the application will be uploaded to the Teams site and submitted to ASRU.** |
| 23/09-08 | Matters relating to the 3RsBMSU* The Midlands 3Rs Symposium was a success and the feedback has been very positive. The Committee thanked the NC3Rs Regional Programme Manager (Midlands) for the organisation of the symposium.
* The talk on zebrafish enrichment was well received and BMSU are hoping to adopt some of the suggested ideas for environmental enrichment in the aquatics facility.
* The 3Rs working group has not met since last AWERB but will be meeting soon.

NC3Rs* Closing date for IAT Andrew Blake Award is 20 October and NC3Rs are sponsoring it this year. It’s for animal technologists who have made significant contributions to improving standards in laboratory animal welfare over the previous twelve months. Winner will receive an invitation to attend the IAT Congress to present a poster on their work and a £250 cash prize.
* Opportunities to join NC3Rs funding panels are open (Partnership and Impact, Studentship and Grant Assessment Panels). They are particularly keen to find people with expertise in big data, but anyone with relevant experience is welcome to apply. Closing date 20 November.
* There is a joint IAT/NC3Rs technicians’ symposium on 18 October. Still places available and attendees get 4.5 CPD credits per day.
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| 23/09-09 | Condition 18 ReportsThere has been one Condition 18 report which has been submitted to the Home Office.  |
| 23/09-10 | Retrospective ReviewThere were no retrospective reviews. |
| 23/09-11 | Any Other Business. The NC3Rs Regional Programme Manager will be handing over the AWERB role to the NC3Rs Head of Academic Engagement and Partnerships who will be attending in future. The AWERB thanked the NC3Rs Regional Programme Manager for their contribution to AWERB. |
| 23/09-12 | Date of Next MeetingDates of future meeting:9th November 2023 via Zoom14th December 2023 in person (Stanley Barnes Meeting Room, Medical School)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 |
| CPD | Continuing Professional Development |
| DVT | Deep Vein Thrombosis |
| HOLTIF |  |
| IAT | Institute of Animal Technology |
| 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 |
| PBM | Photobiomodulation |
| PI | Principal Investigator |
| PIL | Personal licence (Procedure Individual Licence) |
| PPLs | Project licence (Procedure Project Licence) |
| UoB | University of Birmingham |