DRAFT

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

22nd July 2021 (via Zoom)

MINUTES

Present:

21/07-01	Apologies Apologies had been received
21/07-02	Minutes The minutes of the meeting held on 24th June 2021 were considered by the Committee and were approved subject to some minor amendments.

21/07-03	Matters Arising Amendment to licence: Mapping mechanisms for energy homeostasis in rodents. Discussions have taken place and it has been agreed that a new licence application should be submitted rather than an amendment to an existing licence.
21/07-04	Chairperson's Items There were no Chairpersons Items
21/07-05	Verbal Reports from the Director of BMSU and Named Persons In line with rest of University, BMSU is taking small steps to reopening until 16th August when there is no need to Track and Trace. There is a need to maintain BMSU as a functional unit especially due to both annual leave over the summer period along with increasing number of people having to self-isolate due to NHS 'pings'. Situation with regard to the HO re-organisation is still unclear. The following timescales are proposed: • Urgent amendments, turnaround in 5 working days • Other amendments, turnaround in 28 days • Comments on a PPL, within 40 days During this transition period, some licence applications are with the HOI, and some have been submitted to ASRU. Recent health screen shows negative for all agents tested. There was a query on progress in microbiome testing. This is to be progressed once staffing levels are back to normal levels following annual leave. The intra vital suite is busy now, and footfall is beginning to increase.
21/07-06	Report from the Fast Track Procedure Fast Track procedures are progressing.
21/07-07-1	Project Licence Applications *a) Investigating the mechanisms driving cardiac fibrosis and its effect on cardiac function* Summary: The stated aims of this licence were: • to characterise the pathways by which fibrous connective tissue in the heart, termed cardiac fibrosis, leads to cardiac dysfunction and to identify novel therapeutic interventions to prevent or reverse cardiac fibrosis. • The total number of deaths caused by cardiovascular diseases (CVDs) is increasing – by ~21% from 2007-2017. High mortality rates as well as high level of morbidity contribute to the high economic burden of CVDs. The treatment for CVD is increasing

	over time, with prescriptions and operations costs around £6.8 billion in England, the majority spend on secondary care • A protein has been identified called fibroblast growth factor 23 (FGF23) which is associated with the development of cardiac dysfunction in patients with CVDs. • In vitro data suggest that FGF23 can promote accumulation of fibrous connective tissue in the heart. This is likely to contribute to cardiac electrical dysfunction and lead to development of debilitating and lethal heart disease. • It is proposed that interrogation of this new mediator of cardiac electrical dysfunction will illuminate novel cardiac biology insights and therapies targeting cardiac fibrosis and thereby reduce patient suffering and death. The Committee raised the following points: It was confirmed that FGF23 is a very strong biomarker for the disease and arrhythmia. It is difficult to create an arrythmia in a mouse heart, but there are physiological ways of inducing arrhythmias and optical mapping allows these to be observed. Regarding the funding end dates for these studies, some have had extensions, and some are to still be applied for. Dates need to be confirmed. FGF23 stability studies will be undertaken in-vitro to ensure that the protein is stable over the intended period of the study prior to animal work being undertaken. If the mini-pump protocol is not effective, IP injections will be undertaken once per day, although this will be avoided if possible. There were no power calculations in the licence, and it was agreed that further information should be provided. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to being sent to ASRU.**
21/07-07-2	*b) Repairing the damaged spinal cord* <u>Summary:</u> The stated aims of this licence were: • to understand why the nerves of the central nervous system (CNS), and in particular the spinal cord, fails to regenerate after injury, with a view to developing therapeutic agents to counteract this and ultimately preserve function. • Spinal cord injury affects around 1,000 people every year in the UK and an estimated 100,000-1.263 million new cases worldwide, with survivors experiencing life-long loss of function and reduced mobility. • Currently, there are no therapeutic agents that promote axon regeneration after injury and the loss of function that ensues, leaving an urgent medical need for effective therapies. • This application will identify and test therapeutic targets and agents that will promote the regrowth of axons, counteract the negative effects of injury to the spinal cord and ultimately preserve/promote useful function The Committee raised the following points: How do the functional tests and cross-spinal regeneration map to each other and how is spinal regeneration identified compared to normal spinal reflexes. There was discussions of how well rats mimic the situation in humans. Rats have the ability to re-wire spinal circuits, which normally does not occur in humans. Non-animal alternative were considered but are not suitable for the research question being addressed in this licence. However, after discussion, the Committee was satisfied that the rat provides a justifiable model available in the least sentient of animals. Nevertheless, electrophysiology across the lesions will be measured and these measurements correlate to spinal cord recovery. The strain of rats was discussed, and whether an in-bred or out-bred rat should be used. Some rats are less prone to feet biting which can be an issue with spinal injury and loss of feeling in the feet. The preference is to use out-bred rats as they show genetic heterogeneity that is closer to that shown by humans.

	The functional tests were discussed, and the comparisons that are to be recorded between non-injured and injured rats. Injured animals take significantly longer to complete tests, and recovery of neural transmission across the damaged nerve can be measured. It was confirmed that this is categorised as a severe protocol but the animals are cared for by staff who have high level of expertise with the model, and animal numbers are minimal and this needs to be included in the NTS. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to being sent to the ASRU.**
21/07-08	Matters relating to the 3Rs • Following on from the update at the previous AWERB meeting, two videos were shared with the committee showing mice interacting with the trial enrichment items, and the rats exploring the playpen. The BMSU technicians are now observing the rats in the playpen to learn more about which items the rats are engaging with, and that also work practically. • With the support of the university comms team, the two short films are now at the final editing stages. One is focussed on the work of a UoB in vivo researcher, and another focusses on the work of the BMSU more widely. These will be shared with the AWERB once finalised. • Following discussions at the 3Rs Focus Group, the BMSU fish-facility technicians have been looking at a range of enrichment opportunities for the zebrafish. All tanks contain some floating plastic vegetation and a vertical insert has also been trialled to provide some structure inside the tank. The fish have responded positively to this, so it is now being introduced across more tanks and scenarios. • During the 3Rs Focus Group, one of the NVSs raised the possibility that an alternative liquid additive may offer a more refined method of Schedule 1 killing of zebrafish. The experts within the group have agreed to undertake more research with a view to switching if appropriate.
21/07-09	Any Other Business There was no further business.
21/07-10	Date of Next Meeting The date of the next meeting – 2nd September 2021

GLOSSARY

3Rs	Replacement, Reduction and Refinement
ASRU	Animals in Science Regulation Unit
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
CNS	Central Nervous System
CVD	Cardiovascular Disease
FGF	Fibroblast Growth Factor
ECG	Electrocardiogram
HO	Home Office
HOI	Home Office Inspector
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NACWO	Named Animal Care and Welfare Officer
NTS	Non-Technical Summary
NVS	Named Veterinary Surgeon
PI	Principal Investigator
PPLs	Project licence (Procedure Project Licence)
UoB	University of Birmingham