DRAFT

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

13th May 2021 (via Zoom)

MINUTES

Present:

21/05-01	Apologies Apologies had been received
21/05-02	Minutes The minutes of the meeting held on 15th April 2021 were considered by the Committee and were approved subject to some minor amendments.

21/05-03	Matters Arising Provide feedback on 3Rs Strategy for approval at AWERB
21/05-04	Chairperson's Items There were no Chairpersons Items
21/05-05	Verbal Reports from the Director of BMSU and Named Persons BMSU have successfully run the first of the virtual Home Office PIL AB and PIL C. For PIL AB there was an online exam which was audited by the provider. The practical element for PIL C has been undertaken in small groups, with the only outstanding training being the handling section: this will be undertaken on a need basis. The Animal Technicians are still undertaking activity for licence holders which is working well. BMSU still require 5 working days' notice for protocols for planning purposes. NVS weekly visits again. Not a lot of surgery taking place. No health issues at the moment. BMSU is moving forward with frog breeding programme. BMSU is expecting a HOI visit, but no date has been set yet.
21/05-06	Report from the Fast Track Procedure Fast track procedures are in progress as normal and no queries had been raised.
21/05-07-1	Project Licence Applications *a) The Role of Nitrite in Coronary Artery Disease* Summary: The stated aims of this licence were: • to better understand how blood vessels function, and more importantly, how they stop functioning normally when they become diseased and cause a heart attack (myocardial infarction). • Coronary artery disease (CAD) is the leading cause of death worldwide. Currently, there are few treatments available to protect against CAD and there needs to be greater understanding of how blood vessels change when they become diseased. • There are various factors that contribute to the development of CAD and eventually heart attack, this includes high fat diet, diabetes and high blood pressure (hypertension). • Nitrites are known to have beneficial effects on health. However, it is important to know the mechanism of the nitrite pathways so that new therapies can be developed. The Committee raised the following points: The application refers to CAD and heart failure and also to high blood pressure which relates to cardiovascular disease rather than to CAD: the links with nitrite were not clear. The applicant

	clarified the links between blood pressure and nitrite and argued that nitrite treatment can prevent CAD. The scientific background explained in the presentation needs to be clarified in the application. The breeding Protocol states that animals are kept up to 15 months: does the aetiology of heart disease change in older mice? The Committee questioned whether mouse hearts are a good model of human hearts: it was confirmed that they have similar electrical activity even though the ECG looks different. The Committee suggested that the Protocols need to be amended to reflect the scientific outcomes. It was confirmed that osmotic pumps will be used for up to 7 days which is sufficient for the experimental Protocol. The numbers of animals were queried, and it was asked at what point the data collected are classed as 'scientifically significant'. It was confirmed that the average number is 8 animals per treatment group and this is based on power calculations and published work. This information needs to be clarified in the application. The oxygen levels present during the in vitro study was discussed, as the influences of nitrite follow different mechanism depending upon oxygen levels. The applicant confirmed that this will be considered. The issue of transporting animals and stress levels was discussed, and it was confirmed that animals brought into BMSU are all transported in a safe and secure manner by expert transporters. The range of guidelines cited to aid experimental design was queried, specifically the ARRIVE guidelines. The applicant confirmed that all guidance was consulted to ensure best practice and latest techniques were considered. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and that this application will need to be revised and resubmitted to AWERB for further consideration prior to approval.**
21/05-07-2	*b) Developing and Studying Novel Mouse Models of Glioma Development and Progression* <u>Summary:</u> • The aim of this project is to investigate the role of specific genes in glioma development and progression in order to understand the disease process and improve prevention, early diagnosis and treatment options. • Gliomas represent 75% of all primary malignant brain tumours in adults. Because of their malignant behaviour and the fact that they cannot be cured by current therapies, they represent some of the most agressive cancers • Current treatments simply delay tumour progression, resulting in a median survival time of just 12-14 months • Through combined genetic, biochemical and metabolic studies, researchers have begun to uncover some of the early events in the development of brain cancer. • It is now understood that glioma is caused by metabolic disturbances due to alterations in a specific gene called 'IDH1'. This work aims to develop accurate mouse models of glioma by targeting IDH1 alterations to specific brain cells and then to study the role of 2 particular genes in glioma development. The Committee raised the following points: The issue of clear end points was discussed: these need to be clarified in the Protocols, and clearly identified to ensure the animals will not suffer and will be humanely killed as early as possible for the scientific outcome. The symptoms and behaviour of the animals need to be considered to assess adverse effects and humane end points. It was confirmed that the group plans to use a combination of already established and new mouse models. Development of the new models will be guided based on the established models. On this basis, the gliomas should develop in the forebrain rather than randomly within the brain. It was queried how many of the animals will develop hydrocephalus: this was estimated at around 30-40%. There was a query whether development of hydrocephalus would affect the mice prior to the development of the gliomas and whether this would impact the science. There was a query regarding the number of animals used in the pilot study: it was recommended that 1 or 2 animals be used rather than 10.

	Technicians currently monitor the animals on the breeding floor. It was considered whether visual monitoring methods could be used. AWERB recommended that the application be for a 3-year period only and then extended based on the outcome of the pilot study rather than for the full 5-year project. This would also allow for additional funding to be obtained to support the research. The applicant stated that the planned study is based on experience and published literature, and will take advice from the NVS, NACWO and Director of BMSU. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and that this application will need to be resubmitted to AWERB for further consideration prior to approval.**
21/05-07-3	*c) Investigating muscle-organ crosstalk using Adeno-Associated Viruses (AAVs): a proof-of-concept study* <u>Summary:</u> • This is an application for Research Involving Animals Conducted Outside of the UK (Australia). • The work has been reviewed and approved by Monash University Animal Ethics Committee (AEC). • Mice will undergo endurance-type exercise to induce marked release of exosomes into the circulation The Committee raised the following points: The main concern was the term 'exercise to exhaustion' which would be classified as a severe protocol if this were being undertaken in the UK. The applicant confirmed that there is an 'escape' section on the treadmill which allows the animal to stop exercising as needed. Also, the treadmill speed is slowly increased, and the animal exercises for up to a maximum of 90 minutes. This is a pilot study to determine the minimum amount of exercise required to create a release of exosome vesicles from muscle tissue. It was queried why the work is being carried out overseas: it was stated that this a collaborative project and was never planned to be undertaken in the UK. The PI stated that this would have been an opportunity for one of the researchers to travel to the partner laboratory in Australia, but this is not possible due to Covid-19 restrictions on travel. It was queried whether the funder of the project had agreed for this work to be undertaken in Australia: it was confirmed that this had been approved. The NVS proposed that on the basis of the discussion, the project should not be classed as 'exercise to exhaustion', and the terminology should be clarified throughout the application. It was stated that a video of the protocol would be beneficial for AWERB to understand the exercise methodology. The Committee asked for the purpose of the study to be elaborated: it was explained that during exercise there is a release of exosome vesicles, which result in health benefits. However, it is not yet clear where the vesicles are produced, and where the uptake of the vesicles might be. The issue of animal handling was raised: picking up by the base of the tail is not standard protocol within BMSU as it can cause stress to the animal. It was stated that this is the standard handling technique used by the collaborators. The Committee stated that NC3Rs guidance should be utilised. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and the PI, and also stated that videos of the exercise regimes would be required prior to electronic approval.**
21/05-08	Matters relating to the 3Rs • A member of the BMSU attended IAT Congress and identified an item that may provide enrichment for zebrafish. This is now being trialled in the facility to observe how the zebrafish interact with this piece of equipment. • The BMSU apprentices, with the support of a more senior technician, are performing a small study to validate a number of items as providing enrichment for mice.

	• A draft 3Rs strategy document was presented to the committee by the Assistant Director of the BMSU. This document was informed by the results from the 3Rs Self-Assessment Tool and prepared in discussion with the 3Rs Focus Group. Any recommendations from the AWERB committee will be addressed and the final document submitted for formal approval at the next meeting
21/05-09	Any Other Business Members of AWERB have attended the PEL Holders Forum and speaker recordings will be circulated once available.
21/05-10	Date of Next Meeting The date of the next meeting – 24th June 2021

GLOSSARY

3Rs	Replacement, Reduction and Refinement
AEC	Animal Ethics Committee
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
CAD	Coronary Artery Disease
ECG	Electrocardiogram
HOI	Home Office Inspector
IAT	Institute of Animal Technology
IDH1	One of Three Isocitrate Dehydrogenase isozymes
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
PhD	Doctor of Philosophy
PI	Principal Investigator
PIL	Personal licence (Procedure Individual Licence)
PEL	Procedure Establishment Licence
PPLs	Project licence (Procedure Project Licence)
UoB	University of Birmingham