DRAFT

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

14th October 2021 (via Zoom)

MINUTES

Present:

21/10-01	Apologies Apologies had been received
21/10-02	Minutes The minutes of the meeting held on 2nd September 2021 were considered by the Committee and were approved subject to some minor amendments.

21/10-03	Matters Arising No matters arising
21/10-04	Chairperson's Items There were no Chairpersons Items
21/10-05	Verbal Reports from the Director of BMSU and Named Persons New NC3Rs Regional Programme Manager was welcomed to AWERB Three induction refresher sessions have been undertaken and have three people booked into the next session. Induction is required for all people who have not been into BMSU over the lockdown period. There has been a named person meeting, and numbers of users in BMSU are increasing. There are no concerns regarding animal health. The cryogenic team have undertaken the IVF work using frozen sperm, and viable embryos have been produced. Two licences have been awarded by ASRU. There will be a meeting for PEL holders where ASRU will provide an update on how the system is running ASRU audit criteria have been issued, and there are numerous areas that PILs, PELs, PPLs and BMSU need to take into consideration. UoB BMSU audit is unlikely to take place before February 2022 and all those involved will be contacted prior to the audit to Red, Amber, Green (RAG) rate any actions required. Training records will be audited and all PILs need to ensure they have retained and updated their personal records. There will be SOPs for all activities. Occupational Health have a backlog of spirometry testing, which is resulting in a delay in obtaining blue cards for entry to BMSU but this is being addressed.
21/10-06	Report from the Fast Track Procedure Fast Track procedures are progressing with no issues.
21/10-07-1	Project Licence Applications *a) Glymphatic system in the ageing brain* Summary: The stated aims of this licence were: • to characterise the inflammatory and fibrotic changes in the glymphatics system that occur with ageing • The cerebrospinal fluid (CFS) dynamics system in important for maintaining brain stability, and part of this is the glymphatics system which ensures efficient fluid clearance from the brain.

	• Impairments in this system have been observed with ageing and have been associated with age-related diseases such as Alzheimer's disease • Advancing knowledge of age-related changes that occur in the glymphatics system could identify a therapeutic target for treating age-related neurological disorders or limiting the damage of acquired injury in older patients The Committee raised the following points: The justification for the use of a rat model rather than mouse model was discussed. Brain processes and responses do respond differently between rats and mice, however rats are much more translational to brain injury seen in humans. It was noted that the adverse effects section refers to mice and so, this needs to be amended. There was a query regarding brain ageing between healthy and unhealthy brains, and how this is related to inflammation. It was noted that ageing shows some of the characteristics of inflammation and that a base line will be established in this study for CSF flow in young adult and older adult rats. The method of injection was discussed, and glass micropipettes will be used so that there is very little damage around the injection site. This needs to be explained in more detail in the application. The potential failure of drugs that might be used in this model was discussed and the likelihood of the rat model being successfully translated to humans. This needs to be expanded in the application. The title of the application needs to be reconsidered so that it is more specific to the project. Power calculations need to be reviewed and animal numbers need to be justified. This will depend upon a pilot study data. More detail needs to be included in the NTS regarding evidence for why this work is important and explaining the ideas behind the project. There was a query regarding who should be the licence holder for this particular Licence. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to obtaining Chairperson's approval to send to ASRU.**
21/10-07-2	*b) Uncovering novel mitochondrial targets for the management of diabetic retinopathy* <u>Summary:</u> The stated aims of this licence were: • To better understand whether the replacement of damaged mitochondria can reduce sight loss associated with diabetes, and to identify drugs that can be used for this purpose. • 415 million people world-wide are living with diabetes, and diabetic retinopathy (DR) is one of the most common complications (~80%) in those who have had diabetes for 10-20 years. • Even with optimal control of risk factors (e.g. blood-sugar levels), the incidence of DR remains very high, and is aggravated by the lack of effective and safe treatment. • Given the deterioration of mitochondria in diabetes, including the eye (causing DR) and immune system (causing inflammation that exacerbates DR), developing new therapeutics capable of replacing the damaged mitochondria at the systemic level may offer innovative solutions to fight against this visual condition. The Committee raised the following points: The presentation was very clear, and these ideas need to be encapsulated in the application. The terminology used to describe the adverse effects needs to be clarified. Many of the points raised by the NVS, BMSU and the NACWO had already been addressed. Preliminary studies have been undertaken and it was confirmed that all animals exhibit retinal damage. The level of morbidity was discussed. The application stated that there will be up to 35% mortality with animals that have had frank diabetes for between 6 and 9 months. It should be clarified in the application that this is actually an attrition rate rather than a mortality rate. The use of blood tests was discussed, and what will be analysed in the samples. Small volume blood samples will be taken from the tail. Drug delivery is via drinking water and it was queried how the dosage is managed. This is not an ideal way of dosing, but the volumes ingested even out

	over time. A pilot study will be undertaken to confirm that the animals will drink the water containing the drugs, as sweeteners cannot be used. The number of animals required was discussed. Only male animals will used, and of those, half will be wild-type and half, heterozygous. Control animals will be taken from litter mates. It was confirmed that females do not provide reproducible data and will not be used in this study. Functional recovery following drug treatment was raised and it was confirmed that data is obtained from both control animals and diabetic animals. Power calculations and variability was raised, and agreed that more details need to be included in the application. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to obtaining Chairperson's approval to send to ASRU.**
21/10-08	Matters relating to the 3Rs • Dr Prescott stepped down from the AWERB after long service as was thanked by the Committee. Dr Foster was welcomed to AWERB as the new NC3Rs Regional Programme Manager for the Midlands. It was confirmed AWERB members will continue to receive the NC3Rs monthly newsletter. • The NC3Rs has launched two new online resources, one on malocclusion in mice, with posters and slides to help technical staff and researchers spot the signs of malocclusion, and one on organ-on-a-chip technologies, to showcase activities in this area. • Registration is open for a webinar (9 November) on reducing the use of sentinel mice for health surveillance by using environmental monitoring strategies. • The NC3Rs/NCRI survey on rodents in cancer research will be highlighted to the Institute of Cancer and Genomic Sciences. • Skills & Knowledge Transfer Grants provide funding for 3Rs models and techniques to be transferred between laboratories – informal outlines are due 26 November, with an introductory webinar on 2 November; joint awards are available with CRUK. The Project Grants call opens on 3 November, with formal outlines due 11 January (so allow time for university sign-off). • NC3Rs is recruiting for new members of its grant assessment panels – the deadline to apply is 17 November. • The BMSU technicians have worked closely with a research group to switch from the use of wound clips to sutures when closing surgical wounds. This is a refinement as it avoids the difficult task of trying to remove a wound clip from the animal after the wound has healed. • The BMSU is currently housing a group of rats who are benefitting from access to the rat play pen. This particularly beneficial as this is an ageing cohort of animals and so they are being held for a longer period than usual. • The 3Rs Focus Group reviewed its Terms of Reference. No changes were required and so an updated copy was uploaded to the AWERB records. • Two new 3Rs Champions have accepted an invitation to join the 3Rs Focus Group. This ensures the group remains representative. • The new NC3Rs Regional Programme manager has started in post. An introductory email will be sent to all users, plus the wider university research community. The Regional Programme Manager will also be a member of the 3Rs Focus Group.
21/10-09	Condition 18 Reports Two reports have been submitted.
21/10-10	Any Other Business There was no further business.
21/10-11	Date of Next Meeting The date of the next meeting – 2nd December 2021 Zoom

GLOSSARY

3Rs	Replacement, Reduction and Refinement
ASRU	Animals in Science Regulation Unit
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
CSF	Cerebrospinal Fluid
DR	Diabetic Retinopathy
IVF	In-vitro fertilisation
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
PEL	Establishment licence
PIL	Personal licence (Procedure Individual Licence)
PPLs	Project licence (Procedure Project Licence)
RAG	Red / Amber/ Green
SOP	Standard Operating Procedure
UoB	University of Birmingham