DRAFT

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

4th June 2020 (via Zoom)

MINUTES

Present:

20/06-01	Apologies
20/06-02	Minutes The minutes of the meeting held on 23rd April 2020 were considered by the Committee and were approved subject to some minor amendments.

20/06-03	Matters Arising 20/01-05 Suggestion of including a statistician. No-one has yet been identified, and this will remain on the agenda.
20/06-04	Chairperson's Items An issue has been raised about the poor quality of PPLs being submitted for consideration by AWERB. A variety of people including BMSU staff, NACWOs, 3Rs representatives and the NVS are able to offer support and guidance on applications, but not to rewrite applications. This should be made clear to PI. **Action**: Chair to send a reminder email to all licence applicants regarding the expectations of the AWERB Committee
20/06-05	Verbal Reports from the Director of BMSU and Named Persons Plans are being developed on how to re-open BMSU, with restrictions in place, for the recommencement of research. Discussions are ongoing with PPLs. User capacity will be reduced to around 50% with social distancing measures, and PIs are being asked to nominate a maximum of two fully trained people per PPL to enter BMSU. Where possible, procedural work will be carried out by senior BMSU staff. As a result of senior staff undertaking procedural work, there will be no training programme in place for new staff or students. BMSU aim to start ordering mice as of 15th June 2020, and users return to the unit as of week commencing 22nd June. Only trained researchers will be undertaking IVM and the data produced will be provided to BSc research project students for analysis rather than students being trained. The biggest risk for BMSU is the Covid-19 track and trace system which could result in the loss of a whole shift team. Animals will not be able to be collected outside of nominated times (8am until 4pm). It was confirmed that BMSU will not be accessible over weekends.
20/06-06	Report from the Fast Track Procedure Fast track procedures are in progress as normal.
20/06-07-1	Project Licence Applications *a) Defining the role of MYBL2 in breast cancer progression* Summary: • Breast cancer is the most common cancer in women in the UK. 90% of deaths in breast cancer patients are a result of cancer metastasis and drug resistance. • Within the tumour, a small population known as breast cancer stem cells (BCSCs), are responsible for tumour initiation, therapy resistance and metastasis.

	• The aim of this project is to define how MYBL2 levels contribute to stem cell function in vitro and in vivo, and to decipher the mechanism/s by which MYBL2 regulates survival rate, drug resistance and EMT with BCSCs. • This project also aims to exploit this knowledge to determine if manipulation of MYBL2 and/or downstream pathways, is a way to block BCSC function and hence cancer progression. The Committee asked about whether this was a pharmaceutical company sponsored project. It was stated that this needs to be a research licence not a pharmaceutical commercial testing licence. It was clarified that if the data obtained can be published without approval from a company, it is research, whereas if the pharmaceutical company needs to approve prior to publication, it's a commercial testing licence. This project was confirmed as a research licence. Tumour size and end points need to be consistent throughout the application. The Committee asked why imaging and callipers were to be used. It was confirmed that this is to limit the number of times and animal needs to be anaesthetised to undergo imaging. The NTS includes some complex scientific terminology. An explanation of this terminology needs to be included in the body of the licence to ensure the NTS is as accessible as possible. The 'benefits' section is vague in relation to potential new treatments, and more information is needed on what is already known. The Committee asked how the number of animals had been calculated. Power calculations had been undertaken, but the variance on what these calculations were based were no included. The Reduction section should include the estimate numbers of stem cells to justify the number of animals required. The section on adverse effects needs to be updated. It was confirmed that surgical removal of the tumour will be after culling. Justification of the metastasis model being proposed is needed. It was explained that a tumour is removed from one mouse and transferred to another to look at migration of cells. The protocols need clarification to have consistent humane end points. Where the term 'rarely' is used, there is a need to include the probability figures The lay members of the Committee thought that this was a significant procedure on the animal based on the number of interventions and the size that the tumour grows to. Regarding the tumour growth size, it was stated that one of the conditions of the licence is that animals are culled at the earliest opportunity to obtain the relevant scientific data. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI. The project will need to be re-submitted electronically to AWERB for further consideration by the Committee.**
20/06/07-2	*b) Auto immune diseases of the CNS and their treatments* Summary: • At present there are no therapies that reverse the debilitating disease symptoms of MS. • Current treatments are palliative and only provide support to the body's natural defence system (immune system) to fight the consequences of MS rather than tackle the underlying cause. • The project aims to identify and test effective therapeutic agents that change the immune system to fight the development of MS and protect neurons and associated cells. • The aim of this project is to understand how the insulating material around nerves (myelin sheaths) is destroyed by MS, and then to identify and screen agents that are reparative or control the associated symptoms of this disease, with particular attention to neuronal death, loss of myelin, axonal damage and degeneration. The Committee noted that this is a sever model licence renewal and as such a report will be need to be submitted to the Home Office part way through the licence duration. The licence should include a justification as to why rats are to be used rather than mice. It was stated that all preliminary work, and peer reviewed applications of funding, are based on a rat model used elsewhere. Rats also exhibit similar behaviours to humans when there is CNS

	damage. CNS damage in rats does include immobility of the hind limbs but as soon as the animal exhibits hind limb paralysis, the animal is humanely culled. BMSU staff are familiar with working and caring with Experimental Autoimmune Encephalomyelitis (EAE) animals, and provide as much support for the animals as possible e.g. food on the floor, softer bedding, nesting materials etc. EAE is a widely-accepted model for destruction of myelin in diseases, such as MS. The licence should include details of the humane end points. EAE score needs to go to a score of 3. The 1st stage is a limp tail (score 1) whereas score 3 is a hind limb paralysis, but recovery after 3-4 days. The animals have no problems with eating, drinking, or pressure sores. Their behaviour does not change, and they don't indicate any pain. If pain is shown, then opiates can be used. It was suggested that the rat grimace score be included in protocols. Animals are scored daily until they display symptoms, and then scoring becomes more frequent, The Committee asked whether this was a significant breakthrough in treatment. The PI explained the research is progress well from the previous licence and the PI is optimistic that this research will result in a translational treatment to a clinical environment. It was stressed that the harm / benefit discussion in the application need to be very detailed to explain this. **Decision: Committee agree that more discussion is needed between NVS, BMSU, NACWO and PI. The project will be re-circulated for electronic approval and then sent to the HOI.**
20/06-08	Matters relating to the NC3Rs • NC3Rs Regional Programme Managers have been assisting universities with plans for returning to animal research. • NC3Rs training webinars (e.g. mouse handling, systematic reviews, e-learning modules) are available to watch at: www.nc3rs.org.uk/webinars • University of Birmingham NC3Rs Training Fellows attended workshops on grant writing and developing resilience in the research environment. • Applications for Training Fellowships are due on 15 September. • A new hub on tickling rats as a means to improve their welfare has been added to the NC3Rs website. • NC3Rs has published a blog on approaches to evaluating enrichment and is keen to hear from more technicians about their experiences. • Researchers conducting rodent high-yield behavioural experiments are invited to respond to a new survey. • Registration is open for the 3Rs Prize Event, Wednesday 10 June, 4pm (BST). • Advice continues to be provided on funding applications. • The 3Rs working group has met and identified some immediate and longer term actions: Immediate: o An article will be prepared for the BMSU newsletter introducing the members as 3Rs champions and local points of contact for 3Rs issues/ideas. o All users with access to the BMSU will be sent a reminder of the need to use refined handling techniques when picking up mice. Techs are available to support this in-house. o All in vivo researchers will be emailed a reminder about the importance of considering the 3Rs when designing experiments and preparing PPL applications. Links and supporting info will be provided. o Technicians will start wearing name badges to encourage engagement between techs and researchers. The aim is to help promote conversations about their research and the 3Rs. Longer term: o Update to the website is required to include 3Rs case studies and make the information more UoB focussed. o A centrally co-ordinated system for tissue sharing is required. o To consider the possibility of introducing rat play pens
20/06-09	Any Other Business

	Funding for the *Research on Animals Outside of BMSU – IACUC at the NEI/NIH* application (AWERB minutes 19/12-07-02(c)) has now been awarded and the research will commence in the USA.
20/06-10	Date of Next Meeting The date of the next meeting will be 23rd July 2020 at 10.00am, venue TBC, although there may be an additional meeting.

GLOSSARY

3Rs	Replacement, Reduction and Refinement
AWERB	Animal Welfare and Ethical Review Body
BCSCs	Breast Cancer Stem Cells
BMSU	Biomedical Services Unit
BST	British Summer Time
CNS	Central Nervous System
EAE	Experimental Autoimmune Encephalomyelitis
EMT	Epithelial-Mesenchymal Transition
FOI	Freedom of Information
IACUC	Institutional Animal Care and Use Committee
IVM	Intravital Microscopy
MS	Multiple Sclerosis
MYBL2	MYB-relate protein B
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NACWO	Named Animal Care and Welfare Officer
NEI	National Eye Institute
NIH	National Institute of Health
NTS	Non-Technical Summary
NVS	Named Veterinary Surgeon
PI	Principal Investigator
PPLs	Project Licences
UoB	University of Birmingham
USA	United States of America