DRAFT

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

23rd January 2020

MINUTES

Present:

20/01-01	Apologies
20/01-02	Minutes The minutes of the meeting held on 12th December 2019 were considered by the Committee and were approved subject to some minor amendments.

20/01-03	Matters Arising There were no matters arising.
20/01-04	Chairperson's Items There were no Chairperson's Items
20/01-05	Verbal Reports from the Director of BMSU and Named Persons A FOI request for animal numbers and returns has been made. All information will be available on the website. Interviews for 'Talking Heads' for the website are still ongoing. Animal health status is normal following a Home Office inspection. New batch of frogs has been delivered from the US, and they are healthy and starting to feed. A breeding programme will be introduced if necessary. A Home Office course has been run this year. All BSc Biomedical Science project students requiring training now have their licences and projects are ongoing. BMSU are still awaiting confirmation of who has been appointed to the Home Office Inspector role. Two new apprentices are due to start, and are on an Animal Development Pathway. The Home Office Inspector had suggested that AWERB could be strengthened by having a new member with a study design / biostatistical background, and also have 3Rs 'Champions' to support early career researchers.
20/01-06	Report from the Fast Track Procedure Two fast track procedures are in progress.
20/01-07-1	Project Licence Applications *a) Platelet-Immune Cell Interactions in Haemolytic Disease* Summary: • There is currently no effective treatment in haemolytic disease such as sickle cell disease. The absence of treatment is due to the lack of understanding on how thrombosis and inflammation are triggered and amplified. • Platelets and immune cells are activated in haemolytic disease and their activation is associated with vessel occlusion and organ damage. • Patients with haemolytic diseases suffer from delay in wound healing which increases the risk of infection and skin ulcers. • The aim of this project is to understand how platelets are activated in haemolytic diseases and their contribution to inflammation and thrombosis • The project also aims to understand their role in infection and in wound healing in the context of haemolysis

	The Home Office Inspector has provided comments to the PI regarding this application. The Panel confirmed that a mini-pump could not be used for more than two months. A breakdown on animal numbers was discussed, and breeding numbers need to be included. The Panel was concerned that stress can be a factor with patients with sickle disease, and that the injection would be a stress to the animal. It was confirmed that as long as the animals are young, they recover well following injection. It was queried whether the animals could be anaesthetised for the injection, and it was confirmed that the animals react and recover better while conscious. This injection is vital for protein expression. The Panel was asked whether this therapy is suitable and would this therapy be translatable into humans. The Panel asked about pain threshold, associated stress and sickle damage. The animals are hypersensitive, but are treated when they are young. As the mice age, they become more sensitive due to organ damage. All protocols have lots of optional stages. Most treatments are undertaken before mice reach 12 weeks old. The NVS had queries around end points and how long the mice survive beyond them exhibiting illness. Monitoring of the mice include blood counts and assessing the degree of anaemia. The Protocol does not include any pain monitoring, or an indication of how sick the animal needs to be prior to the end point. The breeding programme was discussed, and the number of breeding pairs was raised. This needs to be confirmed. There would need to be a non-conventional breeding programme to keep the number of males required to a minimum. For each experimental protocol there would need to be four groups: sickle and non-sickle and those that have the injection and those that don't. It was queried whether this was a sickle cell model or a haemolytic model. The sickle cell model is the closest model to the humanised model. There needs to be more justification for the model choice and the hydrodynamic treatment. The ethics of the model were raised, and there was no evidence of other models being investigated. The management of this model needs be considered, and the protocol needs to be stripped back to basics and progressed one step at a time. **Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI. The project will need to be re-submitted to AWERB for further consideration.**
20/01-07-2	b) *The Role of Scavenger Receptors in the Development and Progression of Hepatocellular Cancer* Summary: • The commonest form of primary liver cancer is known as Hepatocellular Cancer (HCC). • HCC prevalence is increasing dramatically around the world and it is now the second leading cause of cancer-related deaths globally. • The majority of patients (90%) with HCC have an underlying liver disease which leads to liver scarring. • It is clear that the cancer is protected from the immune system within the scarred liver. • The aim of this project is to understand the role of scavenger receptors in the development and progression of HCC, and to test whether the administration of therapies to block scavenger receptors can stop tumour growth. The Panel confirmed that mice cannot be moved from Protocol 2 to 3. The effect of scavenger knock-out was discussed. The NC3Rs Regional Programme Manager will provide a number of refinement comments for inclusion. It was confirmed that the option of IP and gavage should be considered. The tumour size was discussed, and whether there is a model to monitor this. Humane end points need to be confirmed. It was queried whether liver function could be measured, and it was stated that the liver can have a significant tumour burden before function is affected. The project needs to be able to prove that the intervention is preventing tumour growth, rather than just looking at tumour size at the endpoint. Pilot studies will determine the best age to cull. Male mice only are being used for this licence. This reflects clinical data where there are lower numbers of women who develop HCC compared to men. Regarding timescales, the combination of carcinogen and diet consistently produces tumours after six months.

	The practicalities of mice group size was discussed. Male mice can be aggressive, but it was stated that mice groups can be mixed at weaning. **Decision: Committee agreed in principle, however further discussions will be undertaken between the NVS, BMSU, NACWO and PI. The project will be recirculated for electronic approval.**
20/01-07-3	*c) Intrinsic and Extrinsic Effects on B Cell Differentiation* Summary: • This is the replacement and extension of a current licence. • The production of antibody and memory B cells is crucial to successful protective immunity. B cells are lymphocytes that are best known for producing antibodies in response to infection. • Without B cells, humans and mice are severely immune-supressed. • The function of vaccines is dependent upon the effective production of antibody response and it is important to understand how B cells respond to antigens. • This project will produce data that increases knowledge of how B cells respond to immunisation. The Panel asked for clarification on the injection point. Pilot work has been undertaken regarding injection site, and the best site is the foot, and not the loose skin above the foot. The animal is anaesthetised and the plantar surface of the foot is injected, but not the foot pads. This targets the lymph nodes. It is important to ensure the mouse is not in discomfort. It needs to be clear when limbs are injected and if multiple limbs are injected at the same time, this needs to be made explicit. The issue of analgesics was discussed. Administration of tamoxifen by diet was discussed, comparing IP and gavage. The most refined method possible should be used. The mineral based carrier for tamoxifen can be an irritant. The breeding programme is complex and needs to be considered as animal numbers appear to be very high. It was agreed that there have been some issues with breeding, and this is being worked on. **Decision: Committee agreed in principle, however further discussions will be undertaken between the NVS, BMSU, NACWO and PI. The project will be recirculated for electronic approval.**
20/01-08	<u>Matters relating to the 3Rs</u> NC3Rs Regional Programme Manager activities since November 2019. • Advice provided on two potential NC3Rs project grant applications. One subsequently submitted, one not (in agreement with advice provided). ▪ Support provided to a researcher invited to submit a full application for an NC3Rs Skills and Knowledge Transfer award. ▪ Provided one-to-one EDA training as part of a Royal Society Fellowship application ▪ Provided advice on the justification of animals sections of two MRC and one BBSRC application. ▪ Provided experimental design and 3Rs advice (alongside the BMSU Director) to a researcher who has been invited for interview for a CRUK/overseas fellowship. ▪ Provided face-to-face 3Rs advice on a PPL application. ▪ Identified and invited two animal technicians to be featured as champions in an edition of Tech3Rs (the NC3Rs newsletter aimed at animal technicians). Focus is on a refinement they developed in conjunction with the NVS, highlighting the importance of a team effort. ▪ Provided advice to a researcher who is undertaking collaborative animal work elsewhere in collaboration and is due to present at their AWERB. Provided advice on applying the 3Rs as part of his experimental design. Birmingham's AWERB is aware of this work. ▪ Gave a presentation on the 3Rs in toxicology to a group of MSc Toxicology students (alongside the BMSU Director).
20/01-09	<u>Any Other Business</u>

	There was no further business
20/01-10	Date of Next Meeting The date of the next meeting will be 5th March 2020 at 10.00am in the Stanley Barnes Meeting Room

GLOSSARY

3Rs	Replacement, Reduction and Refinement
AWERB	Animal Welfare and Ethical Review Body
BMedSci	Bachelor of Science in Biomedical Science
BMSU	Biomedical Services Unit
DNA	Deoxyribonucleic acid
FOI	Freedom of Information
IACUC	Institutional Animal Care and Use Committee
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
NPIMR	Northwick Park Institute for Medical Research
NVS	Named Veterinary Surgeon
PETA	People for the Ethical Treatment of Animals
PI	Principal Investigator
UAR	Understanding Animal Research
UoB	University of Birmingham