CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

4th October 2018

MINUTES

Present:

18/10-01 Apologies

18/10-02 Minutes

The minutes of the meeting held on 23rd August 2018 were considered by the Committee and were approved subject to minor amendments.

18/10-03 Matters Arising

In relation to previous minute 18/06-07-3, which related to a fast track application which was referred to the full committee because of the potential ethical and reputational risks, discussions are ongoing with the Birmingham researcher and the researcher in Brazil about how this work might be allowed to go forwards. The researchers have been asked to consider using the smallest possible wound necessary to get the necessary scientific results and the Home Office Inspector has been consulted. It is hoped that the model can be refined to make it acceptable within the UK legislation.

18/10-04 Chairperson's Items

- The Chair attended the recent NC3Rs symposium hosted at the University of Birmingham. The event was well-attended and feedback from attendees was positive.

- A call has gone out for an additional lay member for AWERB and the Chair will be meeting with people who have expressed an interest.

- The University has appointed a new Research Governance and Ethics Manager to fill this now vacant role, to start in December 2018.

- Recruitment has closed for the new BMSU Assistant Director (Transgenics) role. The successful applicant will hopefully be in post by early 2019.

- The BMSU Strategy Committee will be meeting shortly.

- A new Academic Lead for BMSU has been appointed.

18/10-05 Verbal Reports from the Director of BMSU and Named Persons

Report from the Director of BMSU:

- Activities within BMSU are running smoothly.

- The Home Office Inspector has asked any PPL holders with a PPL which expires in 2019 to start to work on their new applications as soon as possible, as the forthcoming changes to the licensing system may lead to some delays.

- A new electronic licensing system will shortly replace ASPeL and the deadline for ASPeL to be taken offline is 19th August 2019. Legacy data will have to be moved onto the new system and the last few existing paper licences are currently being converted into ASPeL forms to make this migration easier. The University of Birmingham will be an initial beta test site for the new system.

Report from the Named Veterinary Surgeon:

- Xenopus frogs are now being successfully bred in-house and there is no longer any need to import them. New housing is being built to support the colony going forwards.

- BMSU staff are trialling plastic weed as environmental enrichment for zebrafish.

Report from the Named Animal Care and Welfare Officers:

- As a refinement to handling practices within BMSU, cardboard tubes have been bought for all mouse cages and expert advice on using them has been sought from another institution. This is

now part of the regular training within BMSU and is being encouraged as best practice by the NACWOs.

- Following a reorganisation of staffing within BMSU, the first and second floors are now running effectively as a single unit with cross-over support.

- Import and export activity is high and animal numbers within BMSU are holding steady.

18/10-06 Report from the Fast Track Procedure

The fast track procedure is up-to-date and a record of matters discussed is stored on the Committee's Collaborate pages.

18/10-07-1 Application Ref TBA – Osteoblast-endothelial interactions regulate bone formation and remodelling

CD248-MMRN2-CLEC14A is a group of genes that work together to control the movement of osteoblasts (the cells that produce new bone) along blood vessels to sites of new bone formation. The overall aim of this project is to assess the role of the CD248-MMRN2-CLEC14A pathway in 1). Normal bone development and turnover and 2). Bone turnover in osteoporosis and arthritis.

This licence will replace part of an existing, very broad licence, which is being broken down into projects to be carried out by three separate postdoctoral researchers.

The PI gave a presentation explaining the application to the Committee.

Mice with their ovaries removed will be obtained from a commercial supplier. They will usually be supplied 7 days post-surgery, which allows sufficient healing time before they are shipped. It was queried whether the supplier's post-operative care will be of the same standard as that in BMSU – this will be confirmed. The expertise to carry out ovariectomies in-house will be developed early in 2019, to avoid having to transport the animals. However, it could be argued that obtaining such animals from a facility which carries out the surgery so routinely is a refinement.

The Committee queried what proportion of the animals will be in each of the three groups. 70-80% will be used in the K/BxN model, 20-30%

in the TNF model and very few in the CIA model (a moderate model, which will not be allowed to reach severe).

Regarding the microCT data, it was explained that a statistical model has been developed with the School of Computer Sciences to allow the detection of subtle changes in bone erosion.

This research group has done extensive work on the scoresheets to be used for humane endpoints and on the use of analgesia – this is seen as best practice and should be emphasised in the 3Rs section of the application.

As all of the models are of polyarthritis, it was queried whether the use of monoarthritis models have been considered. This will be considered and if it is possible it will be submitted as an amendment. However, as the study is looking at systemic effects, monoarthritis models may not be appropriate.

The Committee queried whether ovariectomy is a good model of age-induced osteoarthritis, as it involves the removal of ovaries from young animals. It was explained that an aging model is not used as it is necessary to be able to treat and repair damage and this would be more difficult with aged mice.

The PI was asked to explain why so many administration routes are listed for tamoxifen. It was recommended that the researcher should use gavage rather than the intraperitoneal or subcutaneous routes, in line with best practice within BMSU. Administration via food usually only works with very young mice, and the substance will not dissolve properly in drinking water.

It is understood that TNFdARE mice may become unwell as they get older, and the Committee asked for further information about how this will be handled. It was explained that the colony will be carefully monitored and that animals will be humanely killed as early as possible if they will not be used for experimental purposes. The experimental animals will be scored weekly, their progression will be monitored and they will be humanely killed as soon as possible once they have been used. Arthritis and skin symptoms represent the dominant phenotype and although IBD has been reported in the literature, it has not been seen in previous studies undertaken by the research team. The use of anti-TNF therapy with breeding males has revolutionised this model, making breeding and the maintenance of the colony much less problematic.

It was commented that the NTS is particularly well-written and the PI agreed to allow it to be used as an example for other researchers.

After the PI left the meeting, no further issues were raised.

Resolved that:

The revisions discussed above will be made and incorporated into the application. Once this has been done, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

18/10-07-2 Application Ref TBA – Understanding mechanism of organ-specific anti-fungal immunity

The overall aim of this project is to define how organ-specific specialised immune cells respond to invading fungi and prevent infection.

The PI gave a presentation explaining the application to the Committee.

It was clarified that the PI has worked with the diphtheria toxin model before. She has rarely seen any adverse effects and the animals have recovered very quickly.

The PI explained that the scoresheets for this study are almost ready and will be updated prior to the start of the proposed work.

It was felt that further information should be provided in the section 'Reduction' about statistics and sample size. The fact that fungal burdens are not usually normally distributed must be taken into account in the statistics. Pilot studies will be carried out to ensure appropriate numbers.

The information given during the presentation on the 3Rs should be included in the application form.

As CNS models can be acute, the PI was asked whether there will be some warning before acute symptoms begin. The PI explained that this has not been an issue to date as the models are not taken for enough to become acute.

The antibiotics to be used are the same combination as that which is used as standard in the NHS, and also used widely after chemotherapy, thus maximising the transferability of the findings of the study.

The high mortality rate of fungal infections is linked to their prevalence in immunocompromised patients and the lack of effective drugs. Poor

rates of diagnosis are also an issue as fungal infections are often misdiagnosed as bacterial and patients are given antibiotics which make the situation worse.

The Committee queried the likely timescale of any transferable findings. Findings related to antibiotics could be put into practice quite quickly, as this would just involve changing prescribing recommendations. Other potential therapies will have a longer timeline.

It was explained that all of the work will be carried out in the containment facility; also, most fungi do not spread from animal to animal and the fungi involved do not form spores, which makes cross-contamination extremely unlikely.

If the condition of an animal deteriorates, it will be humanely killed at the earliest point possible. This will be included in the refinements.

Generally, all animals will experience the same degree of infection; however, the exception is intranasal brain infections, which are more variable.

After the PI left the meeting, no further issues were raised. It was agreed that this was a very well-written application.

Resolved that:

The revisions discussed above will be made and incorporated into the application. Once this has been done, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

18/10-08 Matters relating to the 3Rs

An NC3Rs representative was unable to attend so an update will be given at the next meeting.

18/10-09 Any Other Business

Technicians from BMSU will have a stand at the Technical Academy Conference which will be held on 13th November 2018 at the University of Birmingham.

18/10-11 Date of Next Meeting

The date of the next meeting will be 15th November 2018.

GLOSSARY

3Rs	Replacement, Reduction and Refinement
ASPeL	Animals Scientific Procedures e-Licensing
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
CD248-MMRN2-CLEC14A	A group of genes that work together to control the movement of osteoblasts (the cells that produce new bone) along blood vessels to sites of new bone formation.
CIA	Collagen-Induced Arthritis
CNS	Central Nervous System
IBD	Inflammatory Bowel Disease
K/BxN	Serum containing auto-antibodies
microCT	Micro Computed Tomography,
NACWO	Named Animal Care and Welfare Officer
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NTS	Non-Technical Summary
PI	Principal Investigator
PPL	Project Licence
TBA	To Be Announced
TNF	Tumour Necrosis Factor
TNFdARE	Genetically modified mouse model
UK	United Kingdom