CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

15th November 2018

MINUTES

Present:

18/11-01 Apologies

18/11-02 Minutes

The minutes of the meeting held on 4th October 2018 were considered by the Committee and were approved subject to minor amendments.

18/11-03 Matters Arising

- Both of the PPLs discussed at the last meeting have now been granted and are operational.

- Regarding the import/export of animals, it was queried whether Brexit is likely to have any significant impact. It was believed that this is possible, as most breeders are pan-European. The potential difficulties are being considered and it may be that there will be more paperwork to be completed for import/export after Brexit.

18/11-04 Chairperson's Items

No Chair's items were reported.

18/11-05 Verbal Reports from the Director of BMSU and Named Persons

Report from the Director of BMSU:

- This year, for the first time the Home Office has published additional statistics which include the number of wild type animals culled either as surplus or for the provision of tissue. For the University, this equates to approximately 2500 animals – a relatively small proportion of the 1.8 million such animals recorded across the whole of the UK. BMSU keeps a tight control over breeding activity and buys in standard strains to avoid wastage, rather than breeding in-house.

- An FOI has been received which asks for information about any threats from anti-vivisection groups received by the organisation over the last 3 years. No such threats have been received and this will be stated in the response.

- BMSU technicians ran a stall at the recent Technician's Academy open day in the Great Hall, which attracted considerable interest.

- 2 new members of staff have recently joined BMSU.

- The Home Office Inspector will be visiting BMSU next week to carry out the annual risk review with the Establishment Licence Holder and she will also be meeting with the new Head of the College of Life and Environmental Sciences.

- It is hoped that a second Assistant Director (Transgenics) will be in place within BMSU early in 2019.

Report from the Named Veterinary Surgeon:

- The Xenopus frogs continue to thrive and lay well, the eggs needed for experiments within BMSU.

- Notification was given to the Home Office under condition 18 because of a recent instance in which a pilot procedure did not go to plan. There were no animal welfare implications, but it did highlight that a particular protocol will need further consideration and development before further experiments go ahead.

Report from the Named Animal Care and Welfare Officers:

- A technician from another institution has recently visited BMSU to share best practice on the handling of mice using tubes (both cardboard and clear plastic).

- The Intravital Suite will be holding open days on 28th and 29th November and all are welcome to attend.

18/11-06 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.

18/11-07-1 Application Ref TBA – Role of immune system in deep vein thrombosis

The overall aim of this project is to delineate new cells and/or molecules in the immune system that can be successfully targeted to prevent formation of blood clots in veins.

The Home Office Inspector has not yet commented on this application.

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

It was explained that in previous related experiments, the mice have recovered well from surgery and it was difficult to tell them apart from those which underwent no intervention.

The experiments are usually over a maximum of 48 hours, and are very tightly monitored. Appropriate anaesthesia is used throughout the

procedures up to the point of culling. There are always 2 people present during surgery.

10-20% of the animals will be examined in the intravital suite to obtain additional data about the recruitment of cells. After the surgery, the mice will remain unconscious, will be injected with a fluorescent labeller and will then be observed under the microscope. This takes approximately 15 minutes and represents a scientific refinement and reduction, as it allows the maximum amount of data to be obtained from each animal. Intravital work will usually be carried out at 6 hours post surgery. The animals will not regain consciousness before being humanely killed.

It was explained that within 48 hours after the surgery, between 80% and 90% of the animals will have formed a thrombus.

Regarding the use of experimental drugs, the PI clarified that substances to prevent DVT may be administered prior to surgery.

Regarding the involvement of mast cells, one approach will be the use of mast cell deficient mice; another will involve the administration of mast cell membrane stabilisers. It may also be possible to use various types of mast cell inhibitor.

Minor amendments are required to the NTS and it should be reworded where necessary to ensure that it will be understood by a lay reader.

The NC3Rs Midlands Programme Manager will comment on the application from a 3Rs perspective. In particular, the following points were noted:

- The low oxygen incubator will be required for in vitro rather than in vivo work.

- The mice to be singly housed after surgery are male mice and it should be explained why single housing is necessary.

- For multiple injections, subcutaneous administration is considered to be more refined than intraperitoneal. The wording on the choice of route for injections should be revisited and clarified.

- In the section on 'replacement', it should be explained why it is not possible to achieve the study aims without the use of animals and this section should be strengthened overall.

- In the section on 'refinement', refinements specific to the model should be included in addition to the general refinements already stated. The researcher's experience and surgical skill should be

emphasised.

- The frequency of Doppler usage and the accompanying number of instances of anaesthesia should be clarified. A minimum interval between instances should be stated.

It was queried whether it would be possible to use the femoral vein to reduce the welfare impact on the animals. The PI explained that this would not be possible as the femoral vein does not form a thrombus – this should be made explicit in the application.

After the PI left the meeting, the Committee continued its discussions.

The stated humane endpoints need to be clarified. References to 'severe' should be removed as the licence will not fall within the severe category. Some of the wording in the NTS should be revisited from a style perspective.

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.

18/11-07-2 Application Ref TBA – Adiponectin-PEPITEM pathway as a novel regulator of bone formation and remodelling

The aim of this study is to understand how bone loss and growth are triggered in two clinical contexts, osteoporosis and inflammatory arthritis and to apply this knowledge to treat some of the biggest issues for musculoskeletal health such as osteoporotic bone loss. Specifically, the project focuses on how a particular pathway (adiponectin-PEPITEM) can influence bone growth and loss.

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

It was clarified that some of the reagents in the calvarial bone model are as yet untested and pilot studies will be carried out. The mice involved will be 4/5 weeks old and will be monitored very closely.

It was queried why the age-related arthritis model will only use female mice and the PI explained that the established model is based on female mice and only female mice are used by other project collaborators. All other work will be carried out with male mice.

It was felt that it would be helpful to provide further information about the project's statistics and effect sizes.

In the adverse effects, 'rapid weight loss' is stated and the Committee asked what this would mean in practice. It was explained that this is standard Home Office wording and within BMSU it will be interpreted in light of standard practice.

In the collagen model, a booster may be given at day 21. This will not usually give rise to visible effects in the animal and animals will be monitored twice a week and then daily from day 15. Most animals do not develop inflammation prior to administration of the booster. Analgesia will be given if needed.

The use of Freund's Complete Adjuvent carries some risk of ulceration, but cream will be used pre-emptively on the skin to avoid this.

The research group's use of analgesia in arthritis models is not universal practice within the field and is to be commended from a welfare perspective.

Both of the models to be used are polyarthritis models and the Committee queried whether the use of a monoarthritis model would be possible. This is possible and if a monoarthritis model will be used, an amendment to the project licence will be submitted.

Ovariectomies are carried out to induce the age-related changes seen in osteoporosis. This gives the necessary aging effects in a young mouse and avoids the significant welfare issues which arise when using an aged mouse model. Mice which have had ovariectomies will be bought in to start with, but it may be possible to do the surgery in house in coming months.

There is currently no experience within BMSU of either the ovariectomy or calvarial bone models. The student involved in the project will be jointly supervised by an external researcher who does have the necessary experience, allowing best practice to be shared.

It was queried whether it would be possible to monitor the animals with sore feet in a less invasive manner, i.e. with less handling. Whilst this will not be possible due to the need to take scientific measurements, best practice regarding handling will be observed and analgesia will be used.

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.

18/11-08 Matters relating to the 3Rs

Report from the NC3Rs representative

Activities undertaken recently:

- The University has been awarded 2 new PhD studentships from the NC3Rs.
- The NC3Rs Training Fellowship deadline has now passed and 1 submission has been received from Birmingham.
- The NC3Rs Midlands Programme Manager has presented at a recent 'train the trainer' meeting on refined handling.
- Formal thanks were given to BMSU, the NC3Rs Midlands Programme Manager and the speakers for their efforts in relation to the recent symposium.

Upcoming activities will include:

- The NC3Rs is running a study looking at the feasibility of blinding to reduce the bias in experiments and is looking to recruit PPL holders.
- BMSU technicians will be attending a forthcoming mouse handling workshop.
- The NC3Rs Midlands Programme Manager will be giving a presentation to BMedSci students on the 3Rs.

18/11-09 Any Other Business

- In the spirit of openness, BMSU is considering asking project licence holders if they would be willing to allow their NTSs to be published, anonymously, on the University's publically available webpages. NTSs are published on the Home Office website already, but they are not associated with the University. Also, NTSs are already published on the webpages of some other UK universities. The Committee agreed that this would

be a positive development.

- Consideration will be given to the possibility of creating a 360° video tour of the BMSU facility, to be posted on the University's externally facing webpages.

18/11-11 Date of Next Meeting

The date of the next meeting will be 13th December 2018.

GLOSSARY

3Rs	Replacement, Reduction and Refinement
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
C57B/6	Common strain of laboratory mouse used for genetically modified mouse models.
DVT	Deep Vein Thrombosis
FOI	Freedom of Information
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NTS	Non-Technical Summary
PEPITEM	Peptide inhibitor of trans-endothelial migration
PhD	Doctor of Philosophy
PI	Principal Investigator
PPL	Project Licence
TBA	To Be Announced
UK	United Kingdom