

## **CONFIDENTIAL MATERIAL**

### THE UNIVERSITY OF BIRMINGHAM

#### ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

7th March 2019

### **MINUTES**

**Present:**

19/03-01      Apologies

19/03-02      Minutes

The minutes of the meeting held on 24<sup>th</sup> January 2019 were considered by the Committee and were approved subject to minor amendments.

19/03-03      Matters Arising

There were no matters arising. Application still ongoing and ready to come back to the committee in 2-3 weeks

19/03-04      Chairperson's Items

No Chair's items were reported.

19/03-05      Verbal Reports from the Director of BMSU and Named Persons

There was a Users Forum in February with 50-60 people in attendance. An update was given on BMSU and a presentation on tunnel handling. BMSU are encouraging tunnel handling but it is not yet being enforced. Animal Technicians are able to train and advise on an individual basis but additional time needs to be allowed for this. Lot of licensees keen to trial tunnel handling and the NVS is working with research groups to ensure that the same animal is handled in the same way, facilitating the transition to full tunnel handling.

BMSU have enforced the Single use of needles policy. Institute of Animal Technology has made March the Animal Technicians month to recognise the work they do. Several events are being held in BMSU including lunch and learn events for Technicians and also a quiz in aid of Comic Relief which is being opened up to BMSU and Research Teams. BMSU is also participating in Technician of the Month and recognising the whole team.

The Home Office Inspector will visit again towards the end of March. Amendments are being turned around rapidly. Staff are to attend the Inspectors conference to discuss short protocol writing.

A new licence tool is being trialled. Licences applied for after July will use the new software. BMSU are a beta test organisation and the Home

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Office has budget to amend questions following pilot. Lot of development going into it and comments are being fed back.

There have been some staffing changes in BMSU and a Temp is in post until New Core is implemented to establish what support is needed.

Assistant director (Transnetyx) has been appointed.

19/03-06 Report from the Fast Track Procedure

There were no Fast Track Procedures to be reported.

19/03-07 Project License Application

“CAR T-Cell Therapy for Human Cancer: Addressing Regulatory Issues”

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

Summary:

- Existing project licence has grown and this is beyond the remit of the original licence, and is more than an amendment. Answer regulators questions – pre-clinical trial.
- Test whether a potential new therapy for cancer could be safely applied to cancer patients who also have arthritis.
- Explore possible toxic effects of using CLEC14A-specific CAR expressing T-cells in mice with arthritis (a study requested by the MHRA as we seek to take this CAR-based therapy to clinical trial.
- The overall aim of the project is to determine whether cancer patients with arthritis should be included or excluded from treatment with a potential new cancer therapy.

BMSU stated that all models are painful and that “well tolerated” is an inappropriate phrase. The refinements have come through Animal Technologists working with the animals, rather than the researchers. It was queried whether arthritis would be induced followed by T-cell therapy or vice versa. Irradiating the animal reduces immune system which could affect the development of arthritis in the animal so it may be necessary to change the protocol. Suggested pilot study to determine which mechanism works best

The application includes a calculation within the protocol that anticipates 60 mice as a maximum, but it is predicted to be far fewer. Other PIs who have used model, could potentially use numbers as low as 3 per group and that all animal are taken through to 10 days and then culled. There is a requirement to justify the sample size and then extrapolate rather than relying on other research.

It was queried which elements of this research have already been undertaken by other groups at Birmingham. Irradiation and introduction of T-Cells is novel, otherwise model has been used extensively. The reason for irradiation is that patients having treatment for cancer, would also have some form of treatment to deplete their immune system and this protocol is trying to replicate clinical work in the animal model. The T-Cells are not purified, and there will be other immune cells in the treatment.

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It was queried whether this a model of immune arthritis rather than osteo-arthritis and would this be an issue? Also, is there evidence that this antigen is expressed in human? It was stated that this protocol is not transplanting tumours, but is a safety testing study which has been requested by the MHRA

The general health monitoring will include over 20% body weight loss or dysplasia and this is not included in the score sheet. There are humane end points.

It was queried whether handling mice with sore joints was required or could they be just be observed. There is a need to confirm the use of analgesic and adverse effects need to be assessed.

The Committee appreciated seeing the score sheet and how it will be tailored for this study.

The lay summary need to be refined to include where analgesia will be used.

Regarding adverse effects and any increase in toxicity, it was confirmed that all studies would be undertaken in mice as evidence shows this is a suitable translational model.

The PI was asked to clarify why this could not be done in-vitro as there are now a number of 3D models now being used. An explanation as to why in-vitro model would not work needs to be included.

The PI was asked whether a 7 day window following T-Cell introduction is this sufficient? Toxicity in previous studies has been seen in 24-48 hours and it has been decided to cull animals at 10 days at peak of arthritis. The Committee also queried where it would be beneficial to undertake a longer study to see if arthritis will resolve itself, although it was agreed that this model is as requested by MHRA.

**Decision: Committee agreed that this is an important study and has no major concerns and when addressed by the PI, the project will be recirculated for electronic approval.**

19/03-08

### Matters relating to the 3Rs

Early career schemes in Birmingham are taken up well and this should be considered as a news item. Working with press office

An event is taking place on Tuesday 10<sup>th</sup> September at the University of Leicester with speakers and posters from UoB

Attendance at experimental design, randomisation and blinding workshops was encouraged.

Strengthening workshops running at Leicester and being brought to UoB. 3R sections of applications are being strengthen

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There is a forum on handling and the logistics of how to manage handling in protocols and encouraging PIs to work in a different way.

There is a potential studentship and DTP using EDA

There was a query to the NC3R on the mouse numbers required for a 5 year project as compared to a 3 year project. It is difficult to speculate on a long project and difficult to predict animal numbers. MRC and BBSRC suggests using the EDA and proposing animal numbers for year 1 and then build the expectations for subsequent years. Researchers need to justify animal use and samples sizes so that the experiments are powered correctly. Guidance is provided by funders. Funder can request rationale for colony sizes and breeding colony sizes. BMSU state that to maintain a genetically altered colony there is a minimum colony size of 30 to reduce the risk of inbreeding.

Research groups need to justify samples size when choosing experiments. BMSU can provide best practice advice on breeding colonies required for protocols. Funders would prefer robust projects which have calculated animal numbers and that the PI can exhibit confidence in the experimental design.

19/03-09      Any Other Business  
There was no other business to report.

19/03-10      Date of Next Meeting  
The date of the next meeting will be Thursday 25<sup>th</sup> April 2019.

## **GLOSSARY**

3Rs	Replacement, Reduction and Refinement
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
PI	Principal Investigator
CAR	Chimeric Antigen Receptor
CLEC14A	C-type Lectin Domain containing 14A
MHRA	Medicines and Healthcare products Regulatory Agency
UoB	University of Birmingham
DTP	Doctoral Training Programme
EDA	Experimental Design Assistant
ERC	European Research Council
BBSRC	Biotechnology and Biological Sciences Research Council
NVS	Named Veterinary Surgeon