CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

14th December 2023

In-person; 10:00am

MINUTES

### Present:

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| 23/12-01 | Apologies |
| 23/12-02 | MinutesThe minutes of the meeting held on 9th November 2023 were considered by the Committee and were approved. |

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| 23/12-03 | Matters Arising23/11-07-1 *Carotid chemoreflex activity and cardiovascular risk.* The application was amended and submitted to ASRU. This has now been approved.23/11-07-2 *Understanding the role of inflammation in stroke development (amendment).* The amendment has been submitted to ASRU. |
| 23/12-04 | Chairperson’s Items* Updated Terms of Reference have been circulated. There have been some minor amendments to memberships and the Fast Track Committee.
* AWERB Review 2023 had been circulated which is a summary of activity over the past 12 months.
* Congratulations to the Director of BMSU for the smooth transition of the activity undertaken since been in post.
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| 23/12-05 | Verbal Reports from the Director of BMSU, NVS and NACWOsDirector:* Plans and schedules have been put in place over Christmas to ensure all tasks continue to be covered, and welfare will not be affected over this period. No short-term experimental protocols will be started during this time. A new Deputy Director of BMSU has been appointed and will join UoB in February 2024.

NVS:* The issue with the irradiator equipment has been investigated, including inspection by the supplier who also performed a recalibration to ensure this was not a source of concern.
* Anaesthesia training is undertaken in-house. All users requiring training in procedures that involve anaesthesia will first be trained and confirmed as competent in the induction and maintenance of anaesthesia before they are trained in the rest of the procedure.

NACWOs:* NACWOs stated that there was nothing to report.
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| 23/12-06 | Report from the Fast Track ProcedureAll applications are uploaded to Teams for comments and are then progressed. Fast track applications are progressing through the Home Office within 2 weeks at present. |
| 23/12-07-1 | Project Licence Applications1. *Investigating the cellular drivers of lung fibrosis*

SummaryThe project aims to examine the role of tissue resident fibroblasts and immune cells in the progression and persistence of lung fibrosis. * Interstitial lung disease (ILD) is a group of respiratory diseases which together account for over 4 million deaths per year globally. These diseases begin with inflammation of bronchioles, alveoli, and/or microcapillary beds.
* Once inflammation breaks immune tolerance and becomes persistent or chronic, this eventually leads to an exacerbated tissue repair response termed as lung fibrosis.
* The mechanism by which lung fibrosis occurs is unclear. Immune dysregulation is considered a major contributor of lung fibrosis with involvement of both innate and adaptive immunity.
* Tissue resident fibroblasts play an important role in repair and structural modification in a normal lung environment. In response to inflammation-induced growth factors, these cells proliferate and form pathogenic fibroblastic foci which drive fibrosis through the release of collagens and metalloproteinases. Despite these findings little is known about how fibroblasts govern fibrosis. If the mechanisms that underlie this process can be understood, novel ways of therapeutically modulating these cells could be developed.

The Committee raised the following points:* In Protocol 2 it states the administration of substances including cells. It was suggested that cells should be listed as a separate injection. Separate humane end points would then need to be included.
* What do the fibroblasts do to promote the disease? The disease starts as an inflammatory disease, but the trajectory is dependent on the tissue. If the early-stage inflammation can be treated, the fibrosis may not develop further.
* One of the adverse effects listed is that the reagent to be placed at the back of the throat is positioned incorrectly. Reassurance was provided that the likelihood of this happening is minimal, as a specific technique is used to administering the injection and training will be provided by a collaborating establishment to those who need to carry out the injections
* Other adverse effects were discussed. For example, when the cells which work to assist wound healing and metabolism are removed, what effects are noticed? It was explained that when there is an immune response, it is dependent upon the burden of the disease and where it is located. The CAR T-cells localise well: they go directly to the affected tissue and are not found elsewhere.
* The use of tamoxifen to turn genes on and off was discussed. There is some previous experience amongst AWERB members of difficulties using tamoxifen in the models proposed and so it was agreed that use of tamoxifen would be removed from the application and re-submitted as an amendment if needed.
* Humane end points need to be refined for the scoring sheet so that, as well as having an overall humane end point score, there is a humane end point for each adverse effect.
* It was queried how long CAR T-cells persist in the circulation. It was stated that they probably become inactive once they have done their job, but they may persist in bone marrow and the spleen. Technology is being developed to be able to switch off CAR T-cells.
* The power calculations need to be reviewed for consistency. The primary outcome is histological evidence of inflammation in the post mortem tissue. Group sizes were also discussed to ensure appropriate effect sizes.

**Decision: The Committee agreed that minor changes should be discussed between the NVS, BMSU, NACWO and PI prior to the application being amended and submitted to ASRU.**  |
| 23/12-07-2 | 1. *Mechanisms controlling anti-tumour responses in primary and metastatic disease (amendment)*

The amendments include:* During the course of this work, a potential means of enhancing anti-cancer responses through stimulation of T cells has been identified by injecting magnetic nanoparticles and activating them by exposing the mice to magnetic fields.
* This process has been shown to activate cells *in vitro*. It may overcome mechanisms in the tumour that block the activity of T cells and can be readily combined with other treatments.
* Injecting animals with magnetics particles alongside the tumour cell injection that is already permitted. The majority of animals will then be placed in a box emitting a magnetic field for up to an hour daily for up to 3 weeks in order to activate the magnetic particles.
* Animals are not expected to experience any adverse effects beyond the transient pain of the injection itself.
* Independent of the amendment to add injection of magnetic particles, the licence is also being amended to increase animal numbers due to additional funding and an additional protocol added to permit the study of control animals in the absence of tumour induction.

The Committee raised the following points:* There needs to be clarity in Protocol 2, to state that the PI would always inject magnetic particles, but that exposure to magnetic fields is an optional step. It was queried whether animals should be exposed to magnetic fields without having the injection. The proposal is that the injection and exposure will active T-cells.
* There was a query regarding whether animal work undertaken elsewhere and involving magnetic particles followed by exposure to magnetic fields had been shown to be beneficial and whether it had been published. Data are available from a thesis but are not yet published outside of the thesis.
* It was queried what the best route of magnetic particle introduction is, and whether the injection site is dictated by nanoparticle size. There was a query regarding the toxicity of nanoparticles on the mouse, and it was stated that there are no adverse effects.
* It was suggested that Protocols be considered that also permit the study of magnetic particles in animals without tumours, and to investigate whether T-cells are activated by the magnetic field alone, without the injection of magnetic particles.

**Decision 1: The Committee agreed that changes relating to the magnetic-activation should be discussed between the NVS, BMSU, NACWO and PI prior to this amendment being returned to AWERB.****Decision 2: The Committee agreed that the amendments to add an additional Protocol to permit the study of control animals in the absence of tumour induction, and the amendments to Protocols for increases in animal numbers were approved for submission to ASRU.** |
| 23/12-08 | Matters relating to the 3RsBMSU* 3Rs Strategy Review document (informed by use of the 3Rs Self-Assessment Tool) had been circulated. This identifies the current 3Rs successes and where improvements can be made. The Use of Animals in Biosciences document has been reviewed, and the Director of BMSU is confident that the University is meeting all of the requirements which could be evidenced if required.
* The new Deputy Director of BMSU will be the 3Rs lead once in post, and will be summarising the 3Rs activity and what is being achieved.
* Efforts are being made to share and disseminate animals which are unavoidably generated through the breeding programmes. Activities include dissection training, and sperm analysis. The in-house breeding colonies are being reviewed and where colonies are no longer used, they will be frozen down and tissues shared.

NC3Rs* No report.
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| 23/12-09 | Condition 18 ReportsPreviously submitted Condition 18 reports are now being returned from the Home Office. Of those returned, there are no further actions required.There has been one Condition 18 report submitted since the last meeting. |
| 23/12-10 | Retrospective ReviewsOne licence has expired recently that will require a retrospective review to be submitted to the Home Office in the New Year due to it having severe protocols.The Director of BMSU presented on the use of internal retrospective review forms by UoB at a RSPCA conference, and has had several requests from other Establishments to share the types of reviews that are undertaken at UoB. |
| 23/12-11 | Any Other Business. * *Update on 23/08-07-1 Understanding the role of inflammation and fibrosis in conjunctival scarring.* A collaborator has been identified who is currently running the mouse model. Animals do get itchy eyes for approx. 20 mins after administration of the eye drops. Animals are scored immediately after treatment, and 24 hours after treatment. Eye drops are administered daily until the required level of fibrosis is obtained (up to 14 days). At this point, the eye drops can be stopped; the fibrosis is retained for subsequent investigation, but the inflammation and associated irritation will cease. BMSU are reassured that this model could be refined for use at UoB. The amended application will be resubmitted to AWERB.
* A bid is being developed with a number of collaborators to apply for EU funding to develop a single repository of tissue taken from animals that have undergone traumatic brain injury. Each sample would have a complete history and other establishments would apply to use the tissue. This should lead to a reduction in animal use, as some severe protocols would not need to be repeated to obtain tissue. There are potential issues regarding EU / non-EU access and policies to resolve. Consideration needs to be given regarding who is accessing the repository and how acknowledgements are managed in publications resulting from use of the tissue.
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| 23/12-12 | Date of Next MeetingDates of future meeting:7th March 2024 via Zoom18th April 2024 in person (room tbc)6th June 2024 via Zoom11th July 2024 via ZoomAll will be from 10am until 1pm. |

**GLOSSARY**

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| 3Rs | Replacement, Reduction and Refinement |
| ASPA | Animals (Scientific Procedures) Act 1986 |
| ASRU | Animals in Science Regulation Unit  |
| AWERB | Animal Welfare and Ethical Review Body |
| BMSU | Biomedical Services Unit |
| CAR T-cells | Chimeric Antigen Receptor T-cells |
| EU | European Union |
| NC3Rs | National Centre for the Replacement, Refinement and Reduction of Animals in Research |
| NCTO | Named Competency and Training Officer |
| NACWO | Named Animal Care and Welfare Officer |
| NIO | Named Information Officer |
| NTS | Non-Technical Summary |
| NVS | Named Veterinary Surgeon |
| PI | Principal Investigator |
| PIL | Personal licence (Procedure Individual Licence) |
| PPLs | Project licence (Procedure Project Licence) |
| SOPs | Standard Operating Procedures |
| UoB | University of Birmingham |