CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

29th June 2023 (via Zoom)

### MINUTES

### Present:

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| 23/06-01 | Apologies |
| 23/06-02 | MinutesThe minutes of the meeting held on 25th May 2023 were considered by the Committee and were approved. |

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| 23/06-03 | Matters Arising23/05-07-1 *Discovering new ways to treat fungal meningitis* requires further amendment prior to submission to ASRU 23/05-07-02 *Assessing the impact of autoimmune disease associated fibroblasts on anti-tumour immunity* has been amended and submitted to ASRU.23/05-07-03 *Investigating the regulation of lymphocyte activation and function* has been amended and submitted to ASRU. |
| 23/05-04 | Chairperson’s ItemsThere were no Chairperson’s items. |
| 23/06-05 | Verbal Reports from the Director of BMSU, NVS and NACWOsBMSU Academic Liaison is going to change due to retirement. There will be two Academic Liaison Officers, one will predominantly liaise with BMSU Users, and one will liaise with MDS College Board. Both will sit on the BMSU Strategy Committee.Several Retrospective Reviews have been submitted recently and feedback has been received from the Home Office. The PPL holders are to be reminded that the reviews are to be released to the public who do not have access to the Project Licences themselves, and so care must be taken to provide full and clear stand-alone information. The new BMSU Director is now also the Delegate for the Named Person Responsible for Compliance. It is best practice that the person in this role does not hold scientific Project Licences and so one licence has already been revoked, with the other coming to an end once the remaining genetically altered animals have been transferred to another Establishment.The installation of the new cage washer is ongoing. Staff have worked really hard to minimise disruption, and this has also required building work onsite. The contractors have been used before and are familiar with the impact that their work can have on the animals. There has been no negative impact on animal welfare at present, there are no concerns on this or other issues for animals in the main BMSU building. There are also no concerns in the aquatic facility.Two NACWOs attended an Institute of Animal Technology Midlands Branch event. BMSU NACWOs met NACWOs from different establishments and had the opportunity to share best practice e.g., sharing images of the rat play pen, as well as sharing information relating import and exporting difficulties |
| 23/06-06 | Report from the Fast Track ProcedureAll applications are uploaded to Teams for comments and are then progressed. AWERB members were encouraged to engage and contribute with the Fast Track process and respond via Teams. |
| 23/06-07-1 | Project Licence Applications1. *Assessing the efficacy of viral vector-mediated gene delivery to the central nervous system*

SummaryThe stated aim of this project is to establish the efficacy of viral vectors to not only target specific neuronal populations in the brain but also to assess modulation of therapeutic gene targets that are linked to neurodegenerative conditions.* It is estimated that one in six people in the UK have at least one neurological condition, with an estimated 600,000 new cases diagnosed every year. These brain disorders include amyotrophic lateral sclerosis (ALS), Alzheimer’s disease (AD), Parkinson’s disease (PD), Huntington’s disease (HD) and frontotemporal dementia (FTD).
* Currently, there are no treatments for these diseases, which can reverse the damage caused, and only palliative treatments to manage their symptoms are available, leaving an urgent medical need for effective therapies.
* In this project, therapeutic targets will be tested, delivered by gene therapy into the brain and transfection rates in neurons and supporting cells will be measured and ultimately cell specific changes in appropriate target molecules will be determined.
* For most central nervous system (CNS) diseases, gene delivery by direct injection into specific areas of the brain may be the most efficacious way of delivering a therapy.
* The advantage of viral vectors over small molecule drugs is that these can deliver the appropriate therapeutic gene for at least nine months or more after a single injection.

The Committee raised the following points:It was queried whether there is evidence that the gene targets that are being looked at have beneficial effects on the cell types that generate these conditions. In reply it was stated that it is known that DNA damage occurs in all of the degenerative diseases over time. If the DNA damage can be inhibited, no more damage is incurred and there may be a reversal which would promote repair.Adverse effects to the brain injections were discussed, and whether injections into the spinal column are more difficult than into the cerebellum. Stereotactic equipment is currently used by the research groups to inject the spinal cord and brain stem to ensure precision and a single needle tract: there are no discernible adverse effects of this. It was queried whether in stopping the ability of the body to kill cells, there would be a risk of anything growing on the spinal cord or brain. It was confirmed that trials have been undertaken with non-viral vectors and there has been no evidence of growths as the process doesn’t interfere with the ability of the cell to die but dampens down the erratic cell death that occurs in response to injury.There was a query regarding the injections and whether specific cells are targeted. It was confirmed that the viruses that are to be used will only target neurons and will not affect other cells. Intravenous injections rather than direct brain injections were queried however, it was stated that there is a limit to the transfer of the virus into the brain due to the blood-brain barrier, making this route less efficient and requiring greater amounts of virus.Adeno-associated virus (AAV)-based vectors are not initially defined in the benefits section. It was queried whether the EDA had been used to optimize the number of animals. It was also noted that the power calculations provided in the application do not include standard deviations. Information should be included on means and standard deviations to allow sample size calculation. The volume of the injection was queried, and two microlitres was stated as optimal and based on previous experiments. It was confirmed that unilateral injections will be undertaken in the brain. It was queried whether the other hemisphere could be used as a control. It was stated that there are some “bystander” effects on the untreated hemisphere and so they do need to use a control group that has had no treatment.The NTS is still quite technical for lay members and needs to be reviewed.**Decision: The Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to the application being submitted to ASRU. The application will be uploaded to the Teams site at the point of submission.** |
| 23/06-07-2 | 1. *Mechanisms of Bacterial Cancer Therapy: Investigation of the effects of Salmonella enterica spp. on intestinal cancer suppression (amendment)*

The Committee raised the following points:This could have been progressed via the Fast Track process, but it was agreed that it was quicker in this instance to bring to AWERB. The PI is leaving UoB and so wishes to add their new Establishment for secondary availability during the transition period whilst the research is being transferred across. The licence has been submitted to the second Establishment’s AWERB and a few amendments have been suggested to better align with local practice at both sites. The standard breeding wording has been amended which is a requirement when amendments are submitted. One query was around gavage needles. UoB use plastic gavage needles, whereas the secondary Establishment use metal needles. The licence is therefore being amended to remove specific details regarding the material of the gavage needle, but UoB will continue to use flexible plastic needles as is current practice. **Decision: The Committee agreed that the application will be uploaded to the Teams site and submitted to ASRU.** |
| 23/06-08 | Matters relating to the 3Rs* Based on knowledge shared from another university, a new potential refinement will be trialled. This involves providing a blue domed structure to zebrafish tanks as a method of enrichment to promote positive behaviours.
* The International 3Rs Awards take place on 20th July 2023.
* The pre-print guidelines for in vitro work are about to be released, and testers are being sought to check that the guidelines are useable and make sense.
* NC3Rs are looking at how they provide the Regional Programme Manager support. Currently out of 100 establishments, 16 Universities benefit from a manager. The decision has been taken that the model needs to change to ensure that every establishment receives support from the NC3Rs. To this end, the NC3Rs provision is being centralised. The six Regional Programme Managers will be redistributed so that two will focus on experimental design, and the other posts will support across the UK e.g., rather than local webinars, there will be national webinars that everyone can attend. At UoB, the new BMSU Assistant Director role will include an element of 3Rs oversight to ensure that 3Rs-related activities proactively continue.
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| 23/06-09 | Condition 18 ReportsOne condition 18 report has been submitted since the last AWERB meeting. The AWERB acknowledged that whilst the animal model is well managed by the BMSU technicians, it is known to be challenging, and so the committee agreed that the Condition 18 report was not indicative of a larger issue.  |
| 23/06-10 | Retrospective ReviewThe format of Retrospective Reviews was discussed based on feedback received from the Home Office. The PPL holder will be reminded that answers provided in the reviews must be clear and stand-alone, rather than refer back to information in the original project licence. |
| 23/06-11 | Any Other Business. There was no further business. |
| 23/06-12 | Date of Next MeetingThe date of the next meeting TBC |

**GLOSSARY**

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| 3Rs | Replacement, Reduction and Refinement |
| ASRU | Animals in Science Regulation Unit  |
| AWERB | Animal Welfare and Ethical Review Body |
| BMSU | Biomedical Services Unit |
| GA | Genetically Altered |
| EDA | Experimental Design Assistant |
| GSK | GlaxoSmithKline |
| HSE | Health and Safety Executive |
| NAM | New Approach Methodology |
| 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 |
| NTS | Non-Technical Summary |
| NVS | Named Veterinary Surgeon |
| PI | Principal Investigator |
| PIL | Personal licence (Procedure Individual Licence) |
| PPLs | Project licence (Procedure Project Licence) |
| UoB | University of Birmingham |