CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

6th April 2023 (via Zoom)

### MINUTES

### Present:

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| 23/04-01 | Apologies |
| 23/04-02 | MinutesThe minutes of the meeting held on 23rd February 2023 were considered by the Committee and were approved. |

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| 23/04-03 | Matters ArisingThe following application has been submitted to ASRU:23/02-07-1 *Investigating the role of platelets in thrombosis and inflammation during sepsis*The following licence has been submitted and awarded.23/02-07-2 *Preparation of Xenopus laevis egg extract for DNA replication and damage research* |
| 23/04-04 | Chairperson’s ItemsThere were no Chairperson’s Items |
| 23/04-05 | Verbal Reports from the Director of BMSU and Named PersonsThe Director of BMSU is retiring and the current Deputy Director of BMSU will step up into the Director role. The Chair of AWERB thanked the outgoing Director for the time and dedication to the role and welcomed the new Director.A new NTCO has been appointed to BMSU.BMSU users will experience major disturbance over the summer when the lift is replaced in BMSU. It may affect some breeding programmes and users are being advised not to undertake any critical activity during this period. The new cage washer is due to be fitted at the same time to avoid further disruption. Reminders will be sent to BMSU users closer to the time.There are no health screening issues. Filters will be sent off for health screening of the frogs and zebrafish shortly. |
| 23/04-06 | Report from the Fast Track ProcedureA number of fast-track applications have been received and all are being progressed.A fast-track application has been referred to AWERB (see 23/04-07-3 below).The mouse breeding licence and the fish breeding licence will be amended so that they will both be held by the new BMSU Director. |
| 23/04-07-1 | Project Licence Applications1. *Investigating the inflammatory processes that support formation of atherosclerosis in arterial disease*

SummaryThe stated aim of this project is to describe the role of inflammation and thrombo-inflammation (interactions between the blood clotting system and the immune system) in the development of atherosclerosis.* World Health Organisation statistics show that an estimated 17.9 million people died from cardiovascular diseases (CVDs) in 2019, representing 32% of all global deaths. Of these, 85% were attributed to heart attacks and strokes.
* CVDs can be caused by atherosclerosis, which is a chronic inflammatory disease of the artery wall whereby fatty deposits lead to the formation of atherosclerotic plaques which, upon rupture, can cause blood clots that block the arteries in the heart (heart attack) or brain (stroke).
* There is currently no cure for atherosclerosis and a major reason for the lack of appropriate medicines is our poor understanding of the molecules and cells that initiate and support inflammation in the artery wall during plaque formation.

The Committee raised the following points:The presentation and application were very clear. It was queried how close the atherosclerosis processes in mice relate to human disease. It was explained that whilst the mice do not develop vulnerable plaques which result in heart attack or stroke as in humans, the broader pathways are very similar, as are the local environments within which the plaques develop. Implantation of minipumps for long-term drug delivery was requested on the application and so the Committee asked about the overall timescales of the experimental work. It was explained that animals are to be maintained on study for up to 24 weeks, although 12 weeks was more typical. Whilst the pumps are implanted under anaesthesia, and designed specifically for mice, they are of the larger size. The committee discussed this with the applicant and were reassured that based on experience the animals cope well with only minor impacts, and the use of the minipumps removes the need to repeatedly inject the animals to administer the drugs. However, these pumps give delivery of drugs for only 6 weeks. Thus, if drug delivery were required beyond this then the pumps will need to be changed. This raised concerns as replacing implanted pumps can be difficult. Therefore, if this is required, it was agreed that a pilot study should first be undertaken to establish whether this is feasible. It was also queried whether refillable mini-pumps could be viable and this will be investigated.On the other hand, if given over a shorter time frame then the drugs will instead be injected; the number of injections and substances was discussed. It was confirmed that only one substance would be used.The Committee queried whether there were differences between male and female mice in relation to the questions to be addressed in the application. It was explained that there is a difference in disease burden between the sexes, with females developing more advanced disease, but there is also more variability between individuals. The application involves both sexes, and it was confirmed that this will be taken into account in the experimental design. The applicant was asked to include these considerations in the power calculations provided in the application.**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.** |
| 23/04-07-2 | 1. *Investigating the effects of chronic kidney disease on cardiac structure and function*

SummaryThe stated aim of this project is characterising the pathways by which chronic kidney disease leads to cardiac dysfunction and identify novel therapeutic interventions to prevent or reverse these changes in the heart.* Chronic kidney disease affects over 10% of the UK population and is a major but under recognised risk factor for cardiovascular disease.
* As chronic kidney disease progresses, there is increasing cardiovascular mortality due mainly to heart muscle disease – called uraemic cardiomyopathy – rather than atherosclerotic coronary artery disease.
* Previous work established that this heart muscle disease begins at an early stage and worsens in parallel with declining kidney function.
* There are currently only a few recognised treatments that delay but none that prevent the onset of uraemic cardiomyopathy in chronic kidney disease. Mechanisms of disease and treatment are unclear.

The Committee raised the following points:It was queried how dietary addition of adenine induces kidney dysfunction. It was explained that rather than causing damage due to water loss, adenine instead forms uric acid crystals in the kidneys. It was also queried that if the adenine diet is stopped, does the kidney damage reverse. Based on published data, it is thought that the damage arrests but does not reverse. This model is currently used in the facility by another researcher to induce acute kidney damage within a 7-week period, and so it was queried as to whether the same approach would achieve chronic damage (where the animals need to be maintained for 20 weeks). It was agreed that some model development would be required along with pilot studies. However, first indications from tissues obtained via tissue sharing was that this model was appropriate. It was queried whether blood tests could be used to establish and monitor the degree of kidney disease. **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.** |
| 23/04-07-3 | 1. *Development of Novel Antimicrobial Peptides for Tackling Corneal Infection and Antimicrobial Resistance*

This is a referral from the Fast Track Procedure for consideration by the full AWERB committee as Fast Track members raised several issues that required further clarification. SummaryThe overarching goal of this 5-year project is to address two major global health issues, namely infectious keratitis (IK) and antimicrobial resistance (AMR), through the development of novel antimicrobial peptides (AMPs). This work is proposed to take place overseas in Singapore and Canada.The Committee raised the following points:The applicant explained that since submitting the paperwork to the committee, they had decided to exclude the Canadian study for the time being, and only consider the study in Singapore and proposed work at UoB. The committee highlighted that whilst the presentation was clear, this was not reflected in the paperwork submitted to the committee. Whilst the work under discussion has been ethically approved in Singapore, it was queried why this study is not being undertaken at UoB. It was explained that Singapore already has a working model and considerable experience of undertaking this type of work, so the intention was for the PI to learn the model in Singapore and then to bring that expertise back to UoB. It was explained that work of this type would actually need to be undertaken in the containment facility within BMSU and would require considerable dedicated procedural space. It was therefore explained to the applicant that due to limited space this may present challenges with what can be undertaken and how. There is currently an issue in that the PI only holds an Honorary contract with UoB and is therefore unable to apply for a Project Licence to undertake work at this establishment until the funding and UoB employment contract is in place.The studies require administration of eyedrops and so the frequency of administration was queried due to the stress this could cause the animal. It was confirmed that drops will be administered every 2 hours. The humane end points of the study need to be reviewed. It was queried whether analgesia would be administered to the animals. Whilst it was stated that the animals would be treated in the same way as clinical patients the details of this must be described in the paperwork. The issue of singly housing mice was discussed, as this is not standard protocol within the UK without scientific justification. It was agreed that there are a lot of uncertainties around this application, and so it was requested that the paperwork be resubmitted to AWERB. The paperwork needs to include the extra details and clarifications as raised during the meeting so as to ensure that the processes undertaken in Singapore meet the requirements of the UK.Funding deadlines were discussed for future funding applications.**Decision: The Committee requested that the PI complete the relevant UoB paperwork with more detail. Further information must be obtained on the procedures being undertaken in Singapore, including the use of analgesia and that humane end points need to be reviewed. The feasibility of carrying out the protocols at BMSU need to be investigated.** |
| 23/04-08 | Matters relating to the 3RsBirmingham 3Rs focus group* The BMSU will be trialling the use of a water bath in the rat play pen, as this has been reported as a refinement at another unit.
* A new ultrasound machine has been installed at the BMSU. Among other applications, this brings refinement opportunities for tumour measurements and surgical procedures.

NC3Rs* 2023 PhD Studentship competition is accepting outline applications. Deadline for outline submissions is 3rd May 2023, 4pm.
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| 23/04-09 | Condition 18 ReportsTwo condition 18 reports have been submitted since the last AWERB meeting. |
| 23/04-10 | Retrospective ReviewThere were no reviews. |
| 23/04-11 | Any Other Business. An additional AWERB meeting will take place in June to review additional licence applications. |
| 23/04-12 | Date of Next MeetingThe date of the next meeting – Thursday 25th May 2023 via zoom |

**GLOSSARY**

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| 3Rs | Replacement, Reduction and Refinement |
| AMP | Antimicrobial Peptides |
| AMR | Antimicrobial Resistance |
| ASRU | Animals in Science Regulation Unit  |
| AWERB | Animal Welfare and Ethical Review Body |
| BMSU | Biomedical Services Unit |
| CVD | Cardiovascular Disease |
| DNA | Deoxyribonucleic Acid |
| IK | Infectious Keratitis |
| 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 |