CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

Animal Welfare and Ethical Review Body (AWERB)

12th January 2023 (via Zoom)

### MINUTES

### Present:

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| 23/01-01 | Apologies |
| 23/01-02 | MinutesThe minutes of the meeting held on 1st December 2022 were considered by the Committee and were approved. |

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| 23/01-03 | Matters ArisingAll actions have been completed. |
| 23/01-04 | Chairperson’s ItemsThere were no Chairperson’s Items |
| 23/01-05 | Verbal Reports from the Director of BMSU and Named PersonsThe Christmas period was a busy time for BMSU but there were no issues. There were sufficient people to work shifts over the full duration of the Christmas/New Year break. AWERB thanked the BMSU Team for all of the work undertaken over this period.The current NTCO is leaving and a new NTCO has been recruited who will be joining in March 23.One of the apprentices has been appointed into a permanent post within BMSU. There has also been some internal promotion and progression of technical staff.PPL holders need to check their training and competency records in ARMIS which is being rolled out group by group. A step-by-step guide on updating records has been produced and will be circulated. ARMIS is also being transferred overnight to a new server for futureproofing.Every PPL holder needs to complete their Home Office annual returns and upload them into ASPeL where they will be checked prior to submission.A proposal for a Workshop at the IAT Congress has been accepted. This will be a practical class on intradermal stitching, as a refinement.There have been no animal health issues over the Christmas period.BMSU is going through UoB Internal Audit at present. Any audit undertaken by the Home Office is likely to be unannounced, ie with no prior notification, but there are no concerns around this. |
| 23/01-06 | Report from the Fast Track ProcedureUp to date with Fast Track and everything is going through as would be expected. |
| 23/01-07-1 | Project Licence Applications1. *Preparation of Xenopus laevis egg extract for DNA replication and damage research*

SummaryThe stated aim of this project is to induce egg laying in frogs so as to generate sufficient material in the form of egg extract for the in vitro study of the process of DNA replication and DNA damage repair. Stimulation of sperm production and maturation in male frogs to prepare sperm DNA will also be required.* Every cell has to duplicate its DNA before cell division.
* During DNA replication all of the DNA has to be duplicated, just once and without any mistakes.
* When mistakes made during DNA replication are not immediately repaired this leads to mutations, which in turn can lead to development of cancer, and other disorders.
* It is essential therefore that we understand in depth the mechanisms that drive and regulate DNA replication and DNA repair
* The process of DNA replication that happens in *Xenopus* egg extract when duplicating *Xenopus* sperm DNA is remarkably similar to the mechanism of replication happening in human cells. Therefore, we may be able to use *Xenopus* egg extract to discover novel regulators and novel pathways in the future to identify potential targets for cancer therapy and other disorders

The Committee raised the following points:The Refinement section stated that animals are maintained in a saline buffer post-injection of hormone, but no explanation was provided. It was explained that they are kept in this environment for around 20 hours to help prevent infection, and that a mildly saline solution was also known within the industry to help reduce stress with no adverse effects on the animals. The 3Rs section of the application needs to be revisited and amended to more reflective of the information provided during the presentation given to AWERB.It was queried whether there was an adverse effect due to food withdrawal for up to 10 days prior to the eggs being taken, and the scientific reason was queried. It was explained that food withdrawal was required to prevent contamination of the eggs by faeces during collection, and that unlike other species, frogs are usually only fed every 3 days. Whilst there is no confirmed method for determining stress levels in frogs, observationally they appeared normal during the fasting period. Following further discussion, it was confirmed that in practice, food is typically removed for 5 days only, representing one missed feed. AWERB therefore recommended that this 10-day upper limit be reduced in the licence to fasting for a maximum of 5 daysIt was explained that re-use of individual animals as stated in the Licence is requested in order to significantly reduce the number of animals required. During discussion with AWERB it was explained that without re-use, animals would need to be imported from the USA to maintain the supply of large volumes of animals required for this study, and this caused significant stress to the animals. However, if animals were re-used this would require less animals so the supply could be maintained from in-house. The AWERB was in agreement that the impact of re-use upon the animal is sufficiently low that re-use is preferable to importing from overseas**Decision: Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to returning the application to AWERB for further discussion.****ACTION: Chair of AWERB to write to all PPL holders to remind them of their responsibilities regarding timelines for applications and renewal of licences.**  |
| 23/01-07-2 | *b) Investigating the role of bilateral alternating stimulation in aversive memory modification*SummaryThe stated aim of this project is to confirm that alternating stimulation of the left- and right-hand sides of the body (otherwise known as bilateral alternating stimulation; BAS) facilitates the updating of aversive memories.* Eye movement desensitisation and reprocessing (EMDR) critically depends upon the use of bilateral alternating stimulation and is a recommended therapeutic intervention for posttraumatic stress disorder
* This study aims to test the hypothesis that bilateral alternating stimulation facilitates memory updating, and that tickling, which is a positive experience for the rat can be used to make the reminded fear memory less strong.
* This will be followed up to explore the precise biological mechanisms involved by using markers to identify changes in protein levels in known pathways in the brain.
* The objectives are focussed on gaining a better understanding of how fear memories are changed that is likely to relevant to human psychiatric conditions.
* It is reduction in this fear response that we aim to achieve. Rats are being used in the study because the objectives involve behavioural assessments of fear memories that cannot be modelled effectively in less sentient animals.

The Committee raised the following points:The application and presentation were clear and easy to follow. A query was raised about whether this procedure worked better with juvenile or adult rats. It was explained that memory processing changes during maturation, hence adult rats were being used. However, it was suggested that if tickling is started in juveniles this allows animals to become accustomed to this as a positive interaction before it is used as such in the study.The degree of electric stock as an aversive stimulus was discussed, and it was explained that the stimulus strength quoted in this licence is based on previous experience and has been refined over time to ensure it is the minimum required to obtain a scientifically valid response in the rats. The relevance of tickling as an intervention was also questioned. It was explained that the tickling response was a positive interaction and was likened to the use of talking therapy which is used following BAS in humans to reduce the fear memory. Having given a clear verbal description of the behaviours following use of the aversive stimulus, the applicant was encouraged to further reflect this information in the NTS.There was a query about whether the clinical use of eye track / talking therapy could be equated to the use of stroking whiskers and tickling in rats. The translatability between humans and rats of the fear mechanism and associated memories was discussed. It was explained that this application is intended to test a scientific hypothesis in rats which may then be translatable into human patients. A discussion around the biological changes that occur in rats and humans following fear took place, and whether this animal study would produce any viable data. It was explained that this project permits investigation of what happens from the time at which a fear response is first induced as opposed to working with people where behaviour can only be investigated after the response has already been experienced and the fear has been established. The NTS needs to be amended so that the benefits of this research are clearer and to ensure it is written as the correct level for lay understanding.**Decision: There was not a unanimous decision on this application. The Committee agreed that further discussions are needed between the NVS, BMSU, NACWO and PI prior to the application being circulated electronically for approval and being sent to ASRU.**  |
| 23/01-08 | Matters relating to the 3Rs* An academic from School of Dentistry applied for joint BBSRC / NC3Rs funding and has been awarded £200k to enhance capacity and confidence in existing non-animal alternative.
* An ARRIVE Guidelines workshop is being run on 26th January 2023.
* A UoB / NC3Rs PhD student has written up a methods paper for the gateway which is under review and will be published soon.
* A new resource page is available on masking and blinding: [Using masking/blinding in in vivo experiments | NC3Rs](https://nc3rs.org.uk/3rs-resources/using-maskingblinding-vivo-experiments)
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| 23/01-09 | Condition 18 ReportsAll Condition 18 reports are being returned and no further information has been requested. There are no common themes or underlying issues that have been identified. There has been one FOI request relating to numbers. |
| 23/01-10 | Any Other Business. The BMSU website will be updated. The content is ready however there are delays with IT in getting a web developer to re-design and update the site.A grant has been approved to study brain injury in national hunt horses who bang their heads during falls whilst competing. Their veterinary team will collect samples of saliva and blood and the analysis will be conducted at UoB |
| 23/01-11 | Date of Next MeetingThe date of the next meeting – Thursday 23rd February 2023 via zoom |

**GLOSSARY**

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| 3Rs | Replacement, Reduction and Refinement |
| IAT | Institute of Animal Technology  |
| ASPeL | Animals Scientific Procedures e-Licencing |
| ASPA | Animals (Scientific Procedures) Act 2986 |
| ARRIVE | Animal Research: Reporting of In Vivo Experiments |
| ASRU | Animals in Science Regulation Unit  |
| AWERB | Animal Welfare and Ethical Review Body |
| BMSU | Biomedical Services Unit |
| DNA | Deoxyribonucleic Acid |
| EDA | Experimental Design Assistant |
| FOI | Freedom of Information |
| FRAME | Fund for the Replacement of Animals in Medical Research |
| 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 |
| PEL | Establishment licence |
| PI | Principal Investigator |
| PIL | Personal licence (Procedure Individual Licence) |
| PPLs | Project licence (Procedure Project Licence) |
| PREPARE | Planning Research and Experimental Procedures on Animals: Recommendations for Excellence |
| PTSD | Post-Traumatic Stress Disorder |
| UoB | University of Birmingham |