APPROVED

CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)
Extraordinary Meeting

27th November 2025 via Teams

MINUTES

25/09-01	Apologies
25/09-02	Chairperson's Items There were no Chairperson's items.
25/09-03-01	PPL Applications for Consideration: "Immune system interactions that lead to inflammatory arthritis" Summary The project aims to: • Explore the process controlling the movement of immune cells from the blood into tissue and out again in health, and how these go wrong in inflammatory arthritis. • Test the ability of new chemical and cell-based therapies to restore normal immune cell movement. • Immune cell movement from the blood into and through tissues is an important protective response to infection and injury. It is very tightly controlled, likened to security checkpoints, to prevent unwanted inflammatory responses. • Some of these security checkpoints involve communication between immune cells and other cell types, including platelets or cells that live within the tissues (stromal cells). However, many of these security checkpoints are lost in chronic diseases such as rheumatoid arthritis. • This work aims to provide more detailed knowledge on the factors responsible for maintaining these security checkpoints, including exactly how the security checkpoints are altered in inflammatory arthritis, and if certain new chemical/biological or cell-based therapies can restore the normal function of these checkpoints. • Ultimately the aim is to use this knowledge to develop a new type of treatment that treats the cause of abnormal immune cell movement, rather than treating the symptoms that arise from unwanted inflammatory responses in arthritis. The following points were discussed: • Three models of arthritis were discussed; one mono-arthritis model where only one joint is affected and lasts for around 10 days, and two poly-arthritis models where all joints are affected (one of these models lasts around three weeks, whilst the other lasts around 50-70 days and best replicates the human disease). It was queried why all three models are used and not just the one that best replicates the human disease. It was stated that the mono-arthritis model is the most refined as only one joint is affected and does model certain aspects of the human disease, whilst the three-week poly-arthritis model allows for the analysis of the role of different cell types. The more prolonged poly-arthritic model is the less refined due to both its duration and the fact that it affects all the joints but is required for validating findings as it does most closely replicate the human disease. • It was further queried whether an alternative model that has the persistence and chronicity of the planned prolonged poly-arthritis model but additionally retains the innate component for trafficking would be more relevant. It was stated that these other models produce pathology outside of the joint before the onset of arthritis whereas the model chosen is specific to the joints. It was stated that chronicity will be important for later stage work but not for the initial stages. • It was queried whether optimisation of the models has been undertaken as part of the previous study. The relevant data using the mono-arthritis model is about to be published whereby the inflammatory clinical score over 10 days shows changes in monocyte and

	lymphoid trafficking. There is no chronicity in clinical signs of inflammation, but there are subclinical changes that can be investigated. • It was queried why male mice are being used in this study. It was stated that in the field of arthritis, males tend to be used as they exhibit more rapid onset of arthritis, and the disease scores tend to be much higher. With females, there tends to be more variability in terms of onset disease and peak of information. Therefore, initial studies are undertaken using males as less animals are required to obtain robust data, and if a result is observed in male mice, it will be repeated in female mice. It was queried whether there is then a risk that female only results may be missed. It was explained that female-only results were unlikely as the stromal microenvironment data seen in male mice is seen in both male and female human tissues. • The number of animals needed to obtain post-mortem bone marrow for transplantation into other animals was discussed. It was stated that the exact number for this experiment has not been established and conversations will take place with BMSU staff and other researchers who are experienced in the technique. It was explained that following bone marrow transplant, the humane endpoint for weight loss is 18% (rather than the standard 15% normally applied to protocols of this severity). This is based on in-house experience where it is known that animals will lose weight but otherwise remain well. The bone marrow transplant is an optional step, but it was queried whether all animals who are irradiated will also have the transplant. It was stated that if the animal has been irradiated, they will have a transplant and will fully recover prior to inducing arthritis. • Callipers are used to measure joint swelling, and it was queried whether the swelling needs to be quite large before an accurate measurement can be obtained. It was stated that small changes in swelling can be measured over time, but the calliper reading is not the only measurement considered, and there are a number of factors which contribute to the overall scoring of arthritis development (e.g. joint redness, joint inflammation etc). • The number of injections that each mouse will experience was discussed. Each mouse could experience between 1 and 32 injections, but typically 16 to 20. Animals have an injection on day 1 and day 21 to induce arthritis and then up to daily injections of reagents under investigation. The scientific need for this dosing regime was explained. • The NTS was discussed, and clarification was provided that the animals are all young adults when arthritis is induced, and this is via injection of a reagent to create a reaction, rather than by inducing a physical injury. • It was recommended in the NTS that the reasons given for using animals were clarified so they better related to the specific aims of the project. • Some of the terminology in the NTS could be clarified e.g. target and pathway. • The degree of pain experienced by the animals was discussed. In the poly-arthritis models, the animals get prophylactic analgesic, and this doesn't affect the inflammatory response. For the mono-arthritis model, no pain relief is required as the peak inflammation is reached at day 2 and immediately reduces, without reaching a stage where pain is induced. Nevertheless, all animals are monitored and if a humane end point is reached the animal is humanely killed. A refinement regarding the handling of the mice was discussed, referring to an RSPCA paper on refining rheumatoid arthritis mouse models. • Confirmation was sought on blood sampling as reference to adhering to LASA guidelines was included in the licence, but the maximum limits permitted in the guidelines were not specified. It was confirmed that the wording used is standard for BMSU so when there are updates to guidelines, they can be applied straight away rather than amendments having to be applied for. • It was queried whether animals are housed singly and it was confirmed that they are not housed singly unless this is required for welfare reasons. • The power calculations were discussed, and the expected effect size of 10% was queried. It was stated that this was the minimum difference that would be accepted as a true result, hence this had been used for the power calculation. **Decision: The Committee agreed that the application should be amended following discussion between the NVS, BMSU, NACWO and PI, then approved by Chair's actions prior to being sent onto the Home Office.**
25/09-03-02	"Microbe and body rhythm influences on the development of type 1 diabetes" (PPL transfer) Summary The project aims to: • Understand the effect of daily body rhythms on immune cells and germs in the body, and how timing of therapy on cells of the immune system or infection can modulate susceptibility to Type 1 diabetes.

	• Body rhythms can be affected by temperature, light/dark cycles, hormones, bacteria, infection and many other factors. Understanding which factor(s) contribute to changing the cells of the immune system to cause type 1 diabetes will enable the development of new targets for therapy to prevent or delay the development of disease. The following points were discussed: • It was noted that this is a licence transfer and so the licence has already been approved by the Home Office. It was noted however that within the protocols there was opportunity to clarify some of the information provided within the steps and humane endpoints to aid clarity and understanding when working with the licence within the facility. • It was agreed that this is a clear body of work. Polydipsia and avoiding dehydration are mentioned in the licence, but there is no reference to high levels of polyurea which can lead to wet cages and negatively impact welfare. It was stated that monitoring of cage wetness, and frequent cleaning was undertaken at the current Establishment, but it would be beneficial to write this into the licence where measures to monitor, control and limit adverse effects are described. • The licence refers to application of the 3Hs (refining Housing, Handling and Habituation) and it was confirmed that this aims to replace oral gavage with pipette dosing or oral dosing. The mice do try and chew the pipette tips, so alternatives are being investigated. Coating the food for some proteins works well, although there is some variability due to some mice eating more food than others. The frequency of oral gavage with discussed, and it was confirmed that this only occurs once daily; this should be clarified in the protocol as currently there are no limits described. • It was confirmed that genetically altered mice are used so they will develop spontaneous diabetes naturally. Some mice used under this licence lack immune cells that protect the gut barrier and as a result it was stated that these mice are more likely to experience prolapse as they get older. • It was stated in humans that cortisol levels decrease during the day whereas with mice this is reversed as they are more active at night. It was queried whether there is any link between cortisol and diabetes. It was explained that some therapies work better in the morning and some in the evening. • The licence states 25,000 mice over 5 years. There are 4 grants associated with the licence and the animal figures are based on power calculations to include every permutation of experimentation. • The issue of antibiotic administration was discussed. Some foods are available with a single antibiotic which is easy to administer, however for multiple antibiotics there is no direct food readily available. As such some treatment is in food and some in drinking water with sweetener. **Decision: The Committee agreed that the application should be amended following discussion between the NVS, BMSU, NACWO and PI and reviewed via Fasttrack prior to being sent to the current Establishment for approval. The application can then be sent onto the Home Office for approval.**
25/09-03-03	"Understanding glaucoma pathology and the development of new therapeutic strategies" Summary The project aims to: • understand how and why glaucoma develops, and to investigate if the underlying cause of this disease can be treated with new experimental therapies. Glaucoma is a complex disease that leads to blindness, with no current curative therapies. • Glaucoma is a leading cause of blindness, often described as the silent thief of sight due to a lack of warning signs before the visual field becomes affected. • The condition is painless but causes irreversible degeneration of the optic nerve, resulting in vision loss. • No treatments currently target the underlying cause of glaucoma. The following points were discussed: • The Committee asked about the logistics of the bilateral approach and whether it's scientifically required or whether it's a reduction. It was stated that eyes are not independent of each other however the pressure response can differ between eyes so both are induced to allow for averages to be taken and maximise the chances of obtaining statistically robust data with as few animals as possible.

	• It was queried whether the rats lose their sight during this model, and the impact of this if both eyes are affected. It was stated that rats do not rely on eyesight and lose about 30% of their retinal ganglion cells which, in humans, would be a site impediment. The albino rats do not show any change in behaviour due to the loss of sight. • The rat eye is anatomically similar to the human eye, but rats do not rely on their eyesight. It was queried whether this affects the development of glaucoma or the effect of the therapy. It was stated that the system that maintains pressures in both rat and human eyes are similar, only the size is different. • The animal numbers need to be confirmed and clarified in the application. • It was stated that if a new therapy is being tested, this would first be tested in vitro on cells in 2D to establish if there is an effect on the relevant cell type prior to using the animal model. • Animals will undergo repeated anaesthesia and recovery, and it was queried whether each animal will undergo the same number of injections under anaesthesia. At present, each animal undergoes anaesthesia 8 times to induce glaucoma, plus optional imaging work. There is also the development of a TGF-β virus model that could increase the number of injections. • It was stated that 60% of the animals get sufficient increase in intraocular pressure, and it was queried what happens to the remaining 40% that do not show a significant increase. Some animals start with high intraocular pressure, so no increase is observed, but in these cases the eyes and tissues are harvested and studied. • The issue of pain relief was discussion and whether any analgesia was required. Opiates can not be used as it reduces the intraocular pressure, and topical administrations cannot be used as it confounds the therapies that are being tested. The rats normally tolerate the treatment well with no indication that pain relief is required. • Protocol 1 states 30 days of treatment whereas Protocol 2 states 7 days. It was queried whether the duration of Protocol 1 is necessary. It was stated that Protocol 2 would be used initially to establish dosing for Protocol 1. It is expected that Protocol 1 would not exceed 14 days of daily treatment once the pressure has increased. • Reference to an optic nerve injury model was incorrectly made and so this should be removed. • Alongside other justification for the use of rats, the application states that mouse models are unsuitable due to the small size of their eyes and increasing the risk of ocular trauma. It was stated that this is incorrect and should be removed as some research groups do use mouse models for glaucoma. • The volume of injection was queried. It was explained that volumes to be injected will be small and so decompression prior to injection will not be required. **Decision: The Committee agreed that the application should be amended following discussion between the NVS, BMSU, NACWO and PI, then approved by Chair's actions prior to being sent onto the Home Office.**
25/09-04	<u>Any Other Business.</u> There has been one potential non-compliance to report. A batch of 16 female mice were received from a commercial supplier and were used in an experiment which went as planned. When the animals were killed at the end of the study it was discovered that one of the mice had been pregnant and the licence does not allow the use of pregnant animals. A potential non-compliance report has therefore been submitted to the Home Office. Having undertaken an investigation, it was confirmed that the mouse had not been in contact with any male mice whilst in BMSU. The female did not appear visibly pregnant at any stage, and the pregnancy was in a state of reabsorption. The commercial supplier has been informed, and they are undertaking a full investigation. The relevant people within UoB and the Home Office have been informed.
25/08-05	<u>Date of Next Meeting</u> 18th December 2025 29th January 2026 26th February 2026 16th April 2026 28th May 2026 2nd July 2026 6th August 2026 17th September 2026 5th November 2026

	17th December 2027 All will be from 10am until 1pm via Teams.

GLOSSARY

3Rs	Replacement, Reduction and Refinement
ARRIVE	Animal Research: Reporting of In Vivo Experiments
ASPA	Animals (Scientific Procedures) Act 1986
ASRU	Animals in Science Regulation Unit
AWERB	Animal Welfare and Ethical Review Body
BMSU	Biomedical Services Unit
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
PEL	Establishment Licence
PI	Principal Investigator
PIL	Personal licence (Procedure Individual Licence)
PPLs	Project licence (Procedure Project Licence)
TGF-β	Transforming Growth Factor
UoB	University of Birmingham