CONFIDENTIAL MATERIAL

THE UNIVERSITY OF BIRMINGHAM

ANIMAL WELFARE AND ETHICAL REVIEW BODY (AWERB)

30th October 2025 via Teams

MINUTES

25/08-01	Apologies
25/08-02	Minutes The minutes of the meeting held on 18th September 2025 were considered by the Committee and were approved.
25/08-03	Matters Arising There were no matters arising.
25/08-04	Chairperson's Items The Chair welcomed a new NC3Rs representative to the Committee. There has been one meeting of the AWERB Working Group to review the documentation used for work undertaken outside of UoB.
25/08-05	Verbal Reports from the Director of BMSU, NVS and NACWOs Director of BMSU: • A new xenopus rack has been purchased for the aquatics facility and the transfer of animals is going well. This is to replace some of the older equipment. • To ensure compliance with ASPA, it is a statutory requirement that all PIL holders undertake Continued Professional Development. With support from the BMSU Steering Committee, BMSU will be providing mandatory PILh refresher training, to be run early in 2026. • Three new academic PIs will be joining the College of Medicine and Health as part of the 125 recruitment scheme. Details of their animal work will come to AWERB as part of the ethical review process to transfer or obtain the required project licences. • One of the recognised training providers has offered BMSU three free places for AWERB refresher training. If any members of the Committee are interested, they should contact the Director of BMSU. • The Animal Science Committee (ASC) has released a report that recommends that all project licences should have a retrospective review undertaken and a process for implementing lessons learned should be applied. AWERB already undertakes retrospective reviews for all licences which end, irrespective of severity. • The ASC made 16 recommendations, 13 of which were for the Home Office. The other three are: 1. Applicants must include lay members in NTS and retrospective reviews and explore tools for accessing readability, 2. Applicants should engage with further NTS guidance and share within their networks. 3. The establishment should consider self-publishing the NTS and retrospective reviews on their website. • At the annual PELh (Establishment Licence Holder) forum, a presentation by ASRU stated that there will be a focus on AWERBs in 2026, with a particular focus on the role of the committee in Replacement. Outcome focussed measurements will be used to determine committee functionality. NVS: • Quarterly health screen results have been received; these are as expected with very low levels of known pathogens detected. • There have been some issues with one study involving mice on an altered diet. The NACWOs observed that some animals were starting to become subdued. Following discussion with the NVS and advice received, the husbandry has been adjusted so that these animals are kept in a warmer environment. This refinement has been successful and so will be implemented going forward. • Animals undergoing induction of a particular model demonstrated adverse effects not permitted in the Project Licence which resulted in a Condition 18 report (see 25/08-10). Following

	discussion with the Named Persons, it was confirmed an amendment will be sought to better describe potential adverse effects. No further experiments involving this model will be undertaken until the amendment has been approved by ASRU. NACWOs: • No issues to report.
25/08-06	Report from the Fast-Track Procedure • All fast-track applications are uploaded to Teams for comments by AWERB. • "Investigating thrombotic and inflammatory medicators in sickle cell disease" (24/11-07-03) Having obtained successful results, the amendment is to add a second strain of sickle cell disease mice in order to confirm findings. • "Understanding the role of Nicotinamide Adenine Dinucleotide (NAD) synthesis on immune cells" (25/07-07-01). The decision has been made to remove the IV protocol and so as agreed by the Committee, review will proceed via Fast-Track.
25/08-07-01	PPL Applications for Consideration: "Investigating how the interface between metabolic homeostasis and the immune system influences liver cancer developments" Summary The project aims to: • Understand how metabolic pathways in the liver microenvironment can regulate the development and progression of primary liver tumours (hepatocellular cancer (HCC)). • Test whether the administration of therapies to block the cross talk between immune cells and metabolic pathways in the liver can stop tumour growth in the context of liver disease and their potential as an immunotherapy. • It is known that a patient's immune system is critical in fighting cancer and there is experimental evidence that HCC tumours growing in a scarred liver are protected from the immune system. If the process can be reversed, the immune system can then be activated to kill the cancer. • This work will investigate how metabolic changes in the liver, seen in obesity and related liver diseases, actively support cancer growth and block the action of immune cells within the liver. • This work will aim to find new approaches to treat HCC that could help the scientific, medical and pharmaceutical industry develop new drugs and improve patient survival. The following points were discussed: • The toxin-induced model was discussed to better understand the expected level of variability in tumour size and the impact that the different diets have on tumour development. It was stated that on a western diet tumours develop at 6 months, with a significant burden seen by 12 months. Initial power calculations use 12 animals per group, and this considers variability. With the high fat, choline deficient diet, tumours are observed earlier (at 3 months) with a significant burden by 6 months. • The tumour cell injection model was discussed with a query raised around the cohort size and engraftment success rates. It was stated that advice is being sought from other groups who undertake engraftment. Also, pilot studies will be undertaken to establish how successful the grafting model will be. The model has been run in BMSU by other research groups, and the animals engraft well. • It was queried whether both the choline deficient diet and western diet were required to achieve the scientific outcomes. It was stated that the western diet causes a high level of fat infiltration into the liver and little scarring, allowing the study of certain aspects of the disease, whilst the high fat, choline deficient diet causes higher levels of scarring that reflects the longer term patient pathology. • The NTS states that 90% of patients who get tumours have an underlying liver disease. It was queried whether the liver disease will be replicated in the animal model. It was stated that different pathways will be modelled, and the application has the option to run both models with and without liver disease. • The NTS states that some animals are injected at an early stage of life. It was confirmed that this is not before day 14 which would not impact the animals being weaned. Whilst the injection occurs at this early stage of life, this induces genetic alterations that do not start to manifest as tumours until the animals reach adulthood.

	• There were several technical terms in the NTS which weren't defined e.g. metabolic pathways, whether liver fibrosis and scarring are the same and what the therapeutic targets are. • The issue of using only male mice in the toxin-induced model was queried. It was stated that this model is well published, and it has been found that the females do not tend to develop tumours, hence females are not used. It was confirmed that the tumour-cell injection model will use both sexes. • The range of known causes of liver disease was discussed such as damage due to alcohol, viruses or fungal toxins and it was queried whether the model proposed is the most appropriate. It was stated that models of alcohol, and virus induced liver disease do not best reflect what happens in humans. The fungal toxins in humans are extremely geographical and not a widespread driver of primary liver cancer. • The number of potential procedures each animal could undergo in Protocol 4 appeared high. It was queried what percentage of mice would go through all of the steps. It was stated that only around 10% of the animals would run through the whole model. • Due to the duration of some of the experimental work (6-12 months), it was queried whether the PI has sufficient funding to cover the costs for the work. The PI confirmed that there are sufficient funds for the first 12 months and further grants are being applied for. • The section of the application which refers to previous achievements gave publications dated pre-2017. It was stated that a lot of pilot work has been undertaken prior to this application being made, and key receptors and pathways have been identified for this experimental work. • It was stated that the format of references should be rationalised for consistency. **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 onto the Home Office.**
25/08-07-02	"Understanding breast cancer progression" Summary The project aims to: • Find out if breast cancer cells can be eliminated, and stop cancer from returning, by focussing on a specific weakness in cancer cells linked to a gene called MYBL2. This gene plays a role in how cancer cells repair their DNA and cope with stress when they multiply. • Understand more about the cells that survive the treatment after targeting MYBL2 to help identify new ways to eliminate them in experimental work and then in patients. • See how these treatments affect cancer cells circulating in the blood which can spread the disease. • Group patients based on how much MYBL2 the cancer cells have, to see if this can be used to predict who will respond better to certain treatments. The following points were discussed: • It was stated that the presentation was very clear. It was queried what the difference is in the subcutaneous tumour tissue model compared to the metastasis cancer model and why use both models. It was stated that whilst the subcutaneous model creates more consistent tumours, there remains a scientific requirement for the metastatic model to best replicate the clinical situation • The use of the mammary fat pad as an implantation site, and impact of tumour size was discussed, and whether the tumour causes any irritation for the animal. It was explained that the mammary fat pad spreads from the underside of the mouse to around its side. Injections are placed into the pad on the side of the animal, hence the site of tumour growth causes the minimum impact possible. • The potential cumulative impact of the number of injections and gavages was discussed. It was explained that all animals will undergo the same number of dosages and routes irrespective of whether they are in the control group or test group as control reagents must also be administered, however where possible drugs will be combined into a single dose to reduce the number of administrations, and the applicant will also review the total number of doses and frequencies permitted per route, to ensure they are scientifically necessary. • The success rate of engraftment was discussed. It was stated that the engraftment rates vary across each experimental group, and animals can all be injected with the same vial of

	material and develop tumours at different times due to the material being frozen and fragmented. Animals that do no develop tumours do not undergo any treatment. • It was stated that the NTS had a lot of terms which were not clear e.g. pathway and what the definition is in this context. • The weight loss figures were discussed, and whether 20% weight loss is an appropriate humane endpoint or whether 15% would be suitable. It was stated that because of the gavage treatment, mashed food is provided but animals often do not want to eat which results in the slightly higher weight loss. Each gavage tube is lubricated with the drug solvent which is sweet and viscous to reduce the irritation to the mouse. • In Protocol 2, blood sampling is mentioned in the introduction but not mentioned in the steps. It was stated that this should be removed. • In Protocol 2 it states that animals will be imaged but the steps need to be modified to reflect the methodology as used in Protocol 3. • The units of measurements need to be confirmed as some state cm^2 and some state cm^3. • This issue of future funding was discussed, and the PI stated the funding sources and grant applications which are currently in submission. **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 onto the Home Office.**
25/08-08	<u>For Discussion: Sepsis Factsheet</u> • As an AWERB, the Committee are required to perform a harm / benefit analysis prior to any PPL application being submitted to the Home Office under the university's PEL. • At present AWERB are not reviewing any licences that include sepsis models, and there are no indications of any licences being submitted in the immediate future. However, having received literature from two sources expressing opinions regarding the use of animals in sepsis it was agreed that the committee ought to take the opportunity to discuss the evidence presented. • The committee reviewed information available in the two documents, along with expertise provided by members of the committee. • It was stated that any animal model used should reflect the scientific question that is being addressed. It was agreed that all animal work is reviewed to ensure that the work is undertaken ethically and appropriately. • Sepsis models are more likely to be classified as severe models. It was queried whether animals used under severe protocols would require a higher level of care? It was explained that in BMSU all animals, irrespective of model or severity, receive a high level of care and the approaches taken are tailored to the specific requirements of each model. • Having reviewed the evidence provided from both parties, AWERB agreed that whilst replacements continue to be urgently required, this type of in vivo research cannot currently be replaced and there remains a need for in vivo sepsis models to answer important scientific questions of clinical relevance. • The committee agreed that more widely, it is important that decisions around the use of any animal model are evidence-based with strong scientific justification required, in the absence of a suitable alternative, or a more refined model becoming available.

25/08-09	<u>3Rs Update</u>
	• A new representative from NC3Rs joined AWERB from October 2025.
	• At the Annual PELh Forum it was stated that a Replacement Strategy for the use of animals in research is due to be published by the Government later this year. It was stated that indications were that the strategy would acknowledge that necessary animal research will continue to be required, but there will be a strong drive towards accelerating replacement technologies.
	• The strategy will be divided into 3 sections:
	  • The first section will summarise the current situation and outline that in vivo research is required for the foreseeable future.
	  • The second section will be the Strategy itself and there will be around 30 commitments separated into themes such as basic research, translational research etc.
	  • The third section will include timings but only on specific tests where replacements are already in the pipeline. Many of these have been informed by the Medicines and Healthcare products Regulatory Agency (MHRA) adding confidence to the timelines proposed.

25/08-10	Condition 18 Reports There have been two Standard Condition 18 reports since the last meeting: • One animal had received an IV injection of serum and responded as expected, however it was subsequently found dead during the evening checks. This animal had been monitored post-procedure and no obvious cause of death was identified during post-mortem examination. • Two animals had been found dead following a surgical procedure. This was the same procedure for which a Standard Condition 18 report had been submitted previously, where it was confirmed that heavier animals would be used going forward. The most recent animals were therefore of a heavier weight. The PILh was reasonably new to this technique and so as a precautionary measure, the more experienced PPLh/PILh will undertake the next surgery with the NVS and newly trained PILh present as observers to review whether there is any learning that can be shared. Separate reports have been submitted to the Home Office for both these incidents, and so BMSU remains legally compliant.
25/08-11	Retrospective Review There is one retrospective review for the UoB internal process (i.e. where a Project Licence does not have any severe protocols). This report has been uploaded to the AWERB Teams site for review.
25/08-12	Any Other Business. No
25/08-11	Date of Next Meeting 27th November 2025 via Teams (extraordinary meeting) 18th December 2025 via Teams All will be from 10am until 1pm.

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
MHRA	Medicines and Healthcare products Regulatory Agency
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
PELh	Establishment Licence
PI	Principal Investigator
PIL	Personal licence (Procedure Individual Licence)
PPLs	Project licence (Procedure Project Licence)
UoB	University of Birmingham