Home Office

PPL Standard Condition 18 Notification Form

Please use this form to notify the Animals in Science Regulation Unit (ASRU) of procedural-related adverse effects that have exceeded or are likely to exceed the severity limitations or controls described in the project licence. ASRU will use this information to determine whether any further action is required.

Do not use to report:

- adverse effects that are due to non-procedural issues;
- potential non-compliance (report by other means);
- issues without adverse welfare consequences.

If you are in doubt whether or not you need to fill in this form, please contact your assigned Inspector.

Please clearly title your document: **'ASRU_establishment name_PPL number_PPLh surname_date_sc18'** and send to your Inspector (e.g. using cjsm) with the subject heading 'PPL SC 18 Notification PPL [Number] – **Check Home Office's Updated Bridging Ways of Working for updated advice on email addresses and subject headings. Cjsm no longer necessary.**

Establishment Licence name	University of Cambridge Anne McLaren Building
Establishment Licence number	X81BD37B1
Name of PPL holder	Stefan Marciniak
PPL number	PP5789170
Protocol no	08
Protocol title	Phenotyping and pressure monitoring in induced mouse models of Pulmonary Hypertension (Moderate) (Mice)
Severity classification	Moderate
1. Date of incident	24/01/2024
2. Species	Mouse

3. Brief details of study and how the limits or constraints have been breached	<u>To add additional information to CASE ID 232952</u> For this study mice are receiving i.p. injections of either LPS (an extract from the coat of bacteria) or vehicle (phosphate buffered saline) 3 times a week for 6 weeks to create a mild sterile inflammatory response. The mice have mutations in one or both of GCN2 and IL6 and there are also wild-type mice on the study. This is an update on a previous SC18 report with CASE ID 232952. The identity of the mouse which was culled after intraperitoneal injections was mistakenly recorded and the correct mouse was MKAC17.1c. This mouse was given intraperitoneal LPS on the 24th of January 2024 and a few minutes later was found moribund and then culled. The mouse was healthy prior to injection. The weight loss since first injection 2 days prior was -4.2%. Note: No additional mice have been added to this SC18 report. This is simply to correct the mouse identity in the previous SC18 report which said that MKAC17.1a was culled due to health reasons but it was in fact MKAC17.1c who was culled.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Upon consultation with a senior animal technician who performed a post-mortem and NACWO it was decided the likely cause of death was kidney infection.

5. Cause of Problem, if known	A gross postmortem was performed by a senior animal tech and an enlarged kidney was found and it was determined that kidney infection was the likely cause of death. MKAC17.1c received LPS at 0.1mg/kg and is homozygous for deletions in both GCN2 and IL6. We have not previously observed this problem in previous chronic studies in which mice received 0.05mg/kg LPS for 6 weeks or when mice received a single dose of 0.1mg/kg LPS. Given the other mice in this study are not showing the same signs we are working under the hypothesis that MKAC17.1c may have had a pre-existing kidney infection which could have been exacerbated by injection of LPS and the genetic deletion of IL6.
6. Action that has been or will be taken *(For example, formulation of drug changed, supportive treatment given, study design modified). If no action needed, indicate why (for example, none required as study has been terminated and will not be repeated)*	To protect against weight loss which might exacerbate the effect of the LPS all mice will be given supplemental diet gel.
7. Reported by (name)	Max Schwiening
8. Date	26/01/2024

**********For official use**********

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	