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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
Establishment Licence number	X81BD37B1
Name of PPL holder	Nicholas Morrell
PPL number	PP7550697
Protocol no	06
Protocol title	Phenotyping and pressure monitoring in mouse models of Pulmonary Hypertension (Mice)
Severity classification	Moderate
1. Date of incident	24/07/2024

2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	The mouse was treated with tamoxifen at a lower dose with 60 mg/kg instead of the previously used and published dose of 80 mg/kg. Tamoxifen was injected daily for 5 days by ip to induce the knockout of endoglin and induce the disease phenotype. The mouse was supposed to undergo an ip injection of Evans Blue and culled 2 hours after to assess the leakage of the lungs. This was scheduled for 30th July 2024. The mouse weight was measured three times a week. No clinical symptoms and no weight loss were observed. The mouse (NMAV70.2a) was found dead during the morning check by animal technician. The severity score for this mouse is severe, which exceeds the severity score for this protocol which is moderate.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	The animal technician found the dead mouse during the AM checks on Wednesday. We discussed re-evaluating the dose of Tamoxifen (despite already using a lowered dose). The mice seem to be more sensitive to the tamoxifen dose than in the past.
5. Cause of Problem, if known	The most likely cause of the problem was the treatment with Tamoxifen (60mg/kg for 5 days) which leads to the knockdown of endoglin in the endothelial cells, which leads to pulmonary hypertension and/or arteriovenous malformations (AVMs) in the pubic symphysis, which leads to heart failure (as published previously). The mouse did not show obvious cause of death.
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)*	We believe it is an individual mouse problem – increased severity of the disease post-tamoxifen treatment, and we don't anticipate this to happen again. However, we can weigh the mice more frequently, every weekday to prevent suffering and premature death.

7. Reported by (name)	Karolina Kostrzyńska PhD student
8. Date	24/07/2024

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

Inspector's comments and recommendations:

Comments and recommendations	Thank you for submitting this notification and thereby complying with standard condition 18 of your project licence. However, the following points should be taken into consideration: - if weight loss was not observed in the animal which died unexpectedly, please consider other options than just increased weighing to mitigate a repeat issue - if the dose of tamoxifen has already been reduced, please ensure a thorough review of all aspects of this study that may have caused the issue, is also carried out. - please speak with your NVS to determine their advice regards investigation and mitigatory actions Please do inform us of any other related incidents should they occur. The content of this SC18 report has been read by an ASRU Inspector and this matter is now CLOSED.
Inspector name	Nicola Watts
Date	06/08/2024