



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]

Establishment Licence name	University of Cambridge
Establishment Licence number	X81BD37B1
Name of PPL holder	Maria P. Alcolea
PPL number	PP7037913
Protocol no	7
Protocol title	Changes in epithelial cell behaviour in response to tissue perturbations
Severity classification	Moderate

1. Date of incident	Wednesday 30 th March 2022
2. Species	Mouse (MABX44.1c)
3. Brief details of study and how the limits or constraints have been breached	This study plan (SP125688, MA_GS_052_06) includes in total 16 animals that were receiving low doses (40mg/L) of DEN carcinogen via drinking water for 2 months. Towards the end of the DEN treatment Cre transgene expression is activated by Tamoxifen in epithelial cells (using keratinocyte specific promoter) to conditionally knock out Sox9 expression in recombined cells. On the 7th of January the MABX44.1c animal has started DEN carcinogen treatment and received all doses (28) via drinking water. The animal weight was stable throughout. On the 7th and 9th of March the animal received two subcutaneous Tamoxifen injection to induce a conditional deletion of Sox9 transcription factor in epithelial cells. The animal weight went down by 10.7% from max and 1.4% from the baseline which was believed to be the adverse effect of the injections. Since then the animal weight was stable and returned back to the baseline. The animal looked and behaved healthy and caused no health concerns. If animal reaches 10% weight loss the technicians notify user for health concern. Animals are not expected to show any adverse clinical signs as a result of DEN treatment, except for weight loss and incidental tumours such as lipomas as they age. Sporadic liver damage was occasionally observed resulting in early animal collection. As this animal has completed the DEN regime only a month ago, neither is a likely cause of death. For the last two weeks the animal weight was monitored weekly. Animal was also checked every day for any clinical signs or abnormal behaviour.

4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	To alleviate the recovery post Tamoxifen injections the vet has advised to perform subcut rather than intraperitoneal injections and 2 rather than 3 injections in total. This has been considered and study plans prepared as advised. Any concerning animals go back to weighing every other day or daily, if necessary, until the weight is stable again. If the concerning signs do not resolve within 24 hours they are culled. In the event of worsening clinical signs animals will be immediately culled. If vital processes such as eating, defecating and breathing are compromised, as identified in regular inspections, animals are culled immediately. Any animal showing weight loss of 10% will be moved to a mash diet and any weight loss of 15% or more for 2 consecutive days are to be culled immediately.
5. Cause of Problem, if known	Unknown
6. Action that has been or will be taken	Since the cause of death is unknown we are taking caution and collecting a batch of animals from the study plan in the upcoming Tuesday (5 th April 2022). We are aiming to keep 4 animals for aging, but with close monitoring of health
7. Reported by (name)	Greta Skrupskeyte, animal found by Shaun Walton
8. Date	30/03/2022

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	

