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]

Establishment Licence name	University of Cambridge
Establishment Licence number	X81BD37B1
Name of PPL holder	Maria P. Alcolea
PPL number	PP7037913
Protocol no	06
Protocol title	Changes in epithelial cell behaviour over time
Severity classification	Moderate

1. Date of incident	14/06/2022
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	In study plan SP127897, animals were administered a transgene inducing agent (tamoxifen) subcutaneously, at age of P6. There were 5 animals that received the drug on the 6th of June, three of them have not shown any signs of ill health, while one of them was found dead, and the other one has gone missing, both on the 14th of June. Due to their age the animals had not been weaned yet and were caged together with the breeding females. There are two litters and two breeding females in this cage, the male had been removed. This was the first litter of the mother of the dead pups. It is likely that the death of the animals was due to being cannibalised rather than as a consequence of the subcutaneous injection of tamoxifen, unfortunately, as one of them was missing and the other was missing half of the body, we could not analyse the body in search of adverse effects of the procedure.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Yes, we had a meeting with Michiel Plugge to discuss about the adverse effects encountered after injecting the K14Cre-Sox9flox line with Tamoxifen. Together we have designed a strategy to reduce the volume and dose of tamoxifen in future experiments, and amend the licence to include subcutaneous route administration in all protocols as a refinement. To avoid cannibalism, we will limit neonatal experiments to the breeders that have littered before, to be able to predict their behaviour upon littering.
5. Cause of Problem, if known	It is suspected that both pups were cannibalised
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)*	In the past we had adjusted the dose of tamoxifen to have a sufficient gene induction in this model, and found that two subcutaneous injections instead of IP injections, at 5mg/20g was the optimal gene induction and well tolerated, we amended the license to include the subcutaneous route in this protocol. However, the cause of death for these pups is likely to be unrelated to the procedure and we will prioritise using litters from breeders that have previously littered.

7. Reported by (name)	Maria T Bejar
8. Date	15/06/2022

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above. It's difficult to ascertain whether the tamoxifen injections and/or handling the pre weaned mice were contributory factors. Agree with the proposed actions/refinements, you have clearly considered how to mitigate against/reduce future deaths. This SC18 can be considered closed.
Inspector name	Neil Smith
Date	18 Jul 22