



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	08
Protocol title	Epidermal wounding
Severity classification	Moderate

1. Date of incident	Friday 12 th August 2022
2. Species	Mouse (M00827665)
3. Brief details of study and how the limits or constraints have been breached	This study plan (SP129062) consists in the administration of a gene expression modulating substance (tamoxifen) by intraperitoneal injection, followed one hour later by two full thickness excisions - one of 8mm in the back skin, on the dorsal region and another of 3mm in the tail- using sterile biopsy punch and performed under general anaesthesia (isoflurane inhaled). We have performed this procedure several times before in other genetically modified mouse lines without complications or adverse effects On the 8th August, the three mice in this study plan received an IP injection of tamoxifen (10ul/g from a 30mg/ml stock concentration) at 9.30am. At 10.30am, one by one the animals were put down to general anaesthesia, the fur of the back was clipped, they were administered pain relief by subcutaneous injection (buprenorphine 0.1ml at 0.03mg/ml) and then they had a full thickness excision performed with a sterile biopsy punch of 8mm on the back and another of 3mm on the tail. They recovered well from anaesthesia and did not show signs of distress. On the 12th August, 4 days after the procedures, one of the animals was found dead during the morning checks. The notification from the technician -who was performing the daily monitoring of these animals- mentioned that this animal looked quite active and alert the day before she was found dead, and was behaving normally, so this finding was a surprise as there were no signs that prompted us to take any action before this unfortunate event. As there was not an evident cause of the death, the organs of this animal were stored for histologic analysis. .

4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	We will discuss with NVS after the histological analysis and discuss whether additional monitoring measures can be implemented in similar future studies.
5. Cause of Problem, if known	This is the first time we had an animal with complications in this protocol, and the wounds created by the biopsy punch were clean and healing well. Therefore, we speculate that the adverse effect may be due to the combination of the tamoxifen injection, the anaesthesia and the biopsy in this animal. However, as the animal did not show weight loss, or any concerning signs as being hunched or piloerection during the time between the procedures and the date of death, the cause of the problem is not known.
6. Action that has been or will be taken	The organs of this animal were dissected for histological analysis and further investigation. In future studies with this animal line, we will increase the time between procedures (IP injection and skin excision) typically separating them in time for at least 24 hours.
7. Reported by (name)	Maria T Bejar, animal found by Christian Coffaro
8. Date	13/08/2022

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above, and the pathology report. Agree that this death was not directly procedurally related. This SC18 can be considered closed.
Inspector name	Neil Smith
Date	1 Sep 22

