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	08
Protocol title	Epidermal wounding (Mice)
Severity classification	Moderate
1. Date of incident	13/01/2025
2. Species	Mus musculus

3. Brief details of study and how the limits or constraints have been breached	**Keep alive request** In the study plan SP145107, which started on the 10th of December 2024, we subcutaneously transplanted cultured cells bearing individual somatic mutations. These cells were derived from the oesophagi of transgenic mice induced to activate specific mutations. The study aims to analyse changes in cell dynamics after somatic mutations occur in healthy cells and to determine whether these cells can grow and contribute to re-epithelialization/tissue repair in vivo. The ultimate objective is to understand whether mutations, typically present in our ageing tissues, synergize with the wounding process to promote cellular transformation and early tumorigenesis (in line with **Protocol 8 Objective 3; Reveal whether cells re-acquire developmental features during tissue regeneration or tumorigenesis**). Although all five transplanted animals seem healthy and do not show any clinical signs of distress, four of them have started showing a subcutaneous mass at the grafting site (being monitored). Based on our previous experience, and since the cells used were not transformed, we were anticipating that cells carrying individual mutations may only sporadically contribute to microscopic outgrowths (if any at all). Hence, visible swelling/mass formation were not accounted for as an expected outcome/ adverse effect in the PPL. We have sought the advice of our NACWO and NVS in this regard. **Request:** Since the animals appear healthy and do not exhibit any concerning signs regarding their welfare or behaviour, we would like to **keep them alive for one more week (collection on the 23/01/2025) to align with previous grafting collection time points (six weeks post-grafting).** This will allow to analyse these samples together with equivalent time points of different conditions and avoid the need to repeat this experiment unnecessarily.

	The NVS (Sophie Kimpton), after consulting with the animal technicians, **has confirmed that the animals are otherwise well, and has expressed her willingness to support our Keep alive request**. We will now start preparing an **amendment to our licence** to include this possible adverse effect and enable further experiments on this relevant aspect.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	The Gurdon NACWO and NVS have been consulted for advice. Sophie Kimpton (NVS), has reviewed the case and consulted with the animal technicians overseeing animal welfare. **She confirmed that the current clinical presentation of the animals is of no concern and has endorsed this keep-alive request (SC18).** Following analysis of the developed mass in all mice in this study, we will further discuss the adverse effects with the NVS. Due to the type of cells transplanted, we cannot exclude the possibility that the origin of the mass is fibrosis, which will become apparent upon sample collection. Upon discussion with the NVS, we will include any relevant adverse effects in a **PPL amendment** for this specific protocol (Protocol 8: epidermal wounding). This will ensure that we can follow up on this potentially relevant observation with additional experiments.
5. Cause of Problem, if known	The cause of mass development is currently unknown. Although the transplanted cells are mutated, they are single mutants. Equivalent cells are also present in healthy aged epithelium and have not been reported to induce tumour or malignancy formation in the oesophageal epithelium individually. Hence, if the presence of macroscopic tumours is confirmed, we consider this experiment of great importance in unravelling the mechanisms behind the observed phenomenon.

For 6. Action that has been or will be taken	If the request is approved, the animals will be kept under close observation on a daily basis. The animals will be collected on the 23/01/2025 and the masses dissected and further analysed. An amendment to the PPL will be submitted in order to include this adverse effect.
7. Reported by (name)	Davide Rossetti
8. Date	15/01/2024

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	