



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	Designated area within the University of Cambridge, Anne Maclaren Building
Establishment Licence number	X81BD37B1
Name of PPL holder	Brian Huntly
PPL number	PP3042348 (Huntly) Investigation of normal haematopoietic stem cell subversion and the evolution, maintenance and targeting of haematological malignancies.
Protocol no	6

Protocol title	Study of the impact of cell intrinsic and extrinsic alterations on native haematopoiesis during the development and progression of blood cancers
Severity classification	Moderate
1. Date of incident	17/10/21
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	We are studying the role of inducible Crebbp $\pm$ KRas mutations co-operate in the induction of B cell acute lymphoblastic leukaemia (B-ALL). In order to increase the penetrance of an immature B cell phenotype we have crossed these mice onto a Pax5 haploinsufficient background. According to the literature, Pax5 haploinsufficient mice are predisposed to B-ALL, but only in the presence of co-operating events (eg additional leukaemic alleles, delayed exposure to infection). We therefore did not expect any animals of this genotype to present with leukaemia. We have aged a control cohort of Pax5 haploinsufficient mice that have been exposed to 5 doses of plpC at approximately 6 weeks old – this is to control for the plpC exposure in the experimental mice, where it is used to induce expression of mutant Crebbp $\pm$ KRas through the activity of Mx1-Cre recombinase. This animal has been asymptomatic and was last bled on 6th Oct. At that point the WCC was normal at 4.3, but unexpectedly flow cytometry did identify some subtle abnormalities in the peripheral B cells (B200^{lo}CD45^{lo}). Since then we had been specifically observing the mouse, but it remained asymptomatic and we planned to repeat peripheral blood sampling this week (increased frequency to 2 weekly from 4-6 weekly). Despite daily checks by our team during the week and by the AMB technical staff on Saturday 16th October, this mouse was found dead on Sunday 17th October. Autopsy showed moderate splenomegaly, potentially indicative of a haematological malignancy.

4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	N/A
5. Cause of Problem, if known	Mouse was found dead by AMB technician on weekend morning check 17/10/21.
6. Action that has been or will be taken <i>(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)</i>	We will continue to monitor the Pax5 haploinsufficient, plpC-treated cohort by daily inspection and by peripheral blood counts/flow cytometry every 4-6 weeks. Mice exhibiting the B220 ^{lo} CD45 ^{lo} population will be monitored daily by a member of our team and specifically flagged for careful monitoring over the weekend, either by our team or AMB staff. Furthermore, we will increase blood monitoring frequency to weekly to monitor for transformation to acute leukaemia.
7. Reported by (name)	Simon Richardson/Ryan Asby
8. Date	19/10/21

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	