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] – **Check Home Office's Updated Bridging Ways of Working for updated advice on email addresses and subject headings. Cjsm no longer necessary.**

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 haematopi-etic stem cell subversion and the evolution, maintenance and targeting of haematological malignancies
Protocol no	7
Protocol title	[Moderate] 07 Study of the impact of cell extrinsic factors on normal, pre-malignant and malignant haematopoiesis through transplantation (Mice)
Severity classification	Moderate
1. Date of incident	24/01/2023
2. Species	Mouse

3. Brief details of study and how the limits or constraints have been breached	One mouse on study plan SP129142 was found moribund on Tuesday 24th of January 2023. The specific study plan interrogates the competitive advantage of Dnmt3a mutant long term haematopoietic stem cells (LT-HSCs) over their wild type equivalents. As such, mice under this study plan had received a lethal dose of irradiation (on the 28th of September 2022) followed by intravenous injection of a pool of wt and Dnmt3a mutant LT-HSCs. Follow up analyses confirmed successful reconstitution (now at four months post injection, suggesting good long term reconstitution) and normal blood parameters. Once long-term reconstitution has been achieved, no adverse phenotypes are expected in this study. The last regulated procedure on this animal was performed on the 2nd of December 2022. The animal was 32 weeks old at the time of death.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	No advice was deemed necessary as the animal was found moribund and was sacrificed.
5. Cause of Problem, if known	No adverse phenotypes are expected at this stage of the study. This animal had been visually inspected on the previous day by both the AMB staff and the user, with no signs of distress evident. Macroscopic examination upon necropsy did not reveal any obvious abnormalities. The haematopoietic tissues analysed did not indicate a haematological malignancy (for which splenomegaly is an obligate phenotype for example). We do not see any obvious connection to the experimental procedures or the biological implications of this study.
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)*	The remaining animals in this cohort (n=12) were visually inspected for any signs of distress or ill health (none was observed). Their blood parameters are due for a check (within the next two weeks) and any abnormalities will be noted, and any such mice highlighted for further checks and analyses.

7. Reported by (name)	Ryan Asby
8. Date	26/01/2023

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above. There were no pre mortem signs or post mortem findings that identify a definitive cause of the mouse becoming moribund. The correct action was taken in culling this mouse.
Inspector name	Neil Smith
Date	1 Feb 23