



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

Protocol title	[Moderate] 06 Study of the impact of cell intrinsic and extrinsic alterations on native haematopoiesis during the development and progression of blood cancers (Mice)
Severity classification	Moderate
1. Date of incident	26/03/22
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	A mouse on the study plan SP126857 was found moribund on 26/03/2022. Animals on this study conditionally express the <i>Dnmt3a R882H</i> mutation within their haematopoietic stem and progenitor cells, following IP injection with plpC. This mutation alone, does not lead to disease but we and others have found it to alter cellular responses to inflammation and DNA damage, with potential long term implications. In order to assess the effects of this mutation to the haematopoietic system, mice under this study could also eventually go on to receive a mild grade challenge (such as irradiation or inflammation-inducing Il1b). The animal had not demonstrated any previous symptoms of ill health (last visual check was performed on Friday 25th of March 2022). Macroscopic examination upon necropsy did not reveal an enlarged spleen (an obligate phenotype of mice that succumb to AML, a disease in which <i>Dnmt3a R882H</i> is a frequent event). This would be in strong agreement with the timing of mutation induction <1 month since induction, a timeline that would be too short for any study-related disease to develop and none of the mice under this study plan had yet received a mild-grade challenge. The animal technician who identified the mouse noted a slightly enlarged liver upon necropsy but no other abnormalities within the intraperitoneal region. The animal was 33 weeks old upon sacrifice.
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	Unknown. Based on the larger than usual liver, we believe that the animal had developed a liver tumour/disease.

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>	Spleen tissue was harvested to confirm that this was not haematological (AML tumour). Unfortunately, on this occasion, we did not request that the rest of the mouse be placed on formalin and it is not possible to further comment on the cause of death. We will amend the wording of future study plans (as well as communicate this to the AMB team) to request that the entire animal is placed in a formalin pot so that tissues can become available for any other analyses. We speculate the death was not related to the study and possibly due to liver disease.
7. Reported by (name)	George Giotopoulos/Ryan Asby
8. Date	28/03/21

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted above, and concur with the conclusions. The cause of this animal becoming moribund is uncertain, and should be considered unexplained. This SC18 can now be considered closed.
Inspector name	Neil Smith
Date	12 Apr 22