

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 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 (Mice)
Severity classification	Moderate

1. Date of incident	26/07/2022
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	A mouse on study plan SP126857 was found dead on 26/07/2022. 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 Monday 25th of July 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) and no other abnormalities were observed. The last regulated procedure on this animal was performed on the 7th of March 2022. The animal was 56 weeks at the time of death.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	In this instance, we did not identify a need to reach out for advice as we deem the cause of death to be unrelated to the experimental procedures and is most probably age related.
5. Cause of Problem, if known	Unknown (likely to be age related). Macroscopic examination of the animal did not reveal any obvious abnormalities (such as splenomegaly, hepatomegaly or lymphadenopathy). No tissues were sent for histology as the animal was found dead.

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>	A necropsy was performed on this animal and did not reveal an obvious cause of death. The remaining animals on this study plan were inspected and did not demonstrate any signs of disease/discomfort (of note, the remaining animals have now been sacrificed and our downstream analyses, as well as a necropsy at the time of death, have not revealed any signs of disease). We cannot think of a reason this death would be related to our study.
7. Reported by (name)	George Giotopoulos
8. Date	28/07/2022

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above. With no prior clinical signs and no conclusive post mortem findings this death is unexplained. This SC18 can be considered closed.
Inspector name	Neil Smith
Date	17 Aug 22