FD-S221825

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	University of Cambridge
Establishment Licence number	X81BD37B1
Name of PPL holder	Brian Huntly
PPL number	PP3042348
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	15/7/22
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	We are investigating the role of CREBBP loss in B acute lymphoblastic leukaemia. In establishing these novel models we have piloted a number of crosses between our existing transgenic models. We have a small cohort of GEMMs engineered to have inducible loss of Crebbpfl/fl under CD19-Cre on a constitutive Pax5 haplo-insufficient background. Unlike our crosses using the Mx1-Cre, none of the CD19 cre mice have yet succumbed to B-ALL. We have been aging a small cohort to establish whether this is either due to genetic non-permissivity or long latency of disease. In this case mouse HUAW2.3e was found dead on 15th July at the age of 78w 5d. It had been reviewed daily during the preceding week by our group (in addition to the daily checks by the animal holding facility) with no concerns noted. It had last been bled on 30th June with a normal FBC. There was no macroscopic evidence of disease on autopsy.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	We believe this animal succumbed to old age with no evidence of haematologic malignancy on recent blood tests or macroscopic autopsy.
5. Cause of Problem, if known	A post mortem has been conducted. Although tissues were decomposed and unsuitable for histology, we were able to note the absence of splenomegaly or other evidence of tumour (e.g. lymphadenopathy), an obligate phenotype B-ALL and related lymphoid disorders. Given the lack of phenotype in this genetic cross we believe this animal died of old age.

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)*	We will bleed the remaining mice from this cohort shortly. If there remains no evidence of disease, we will cull the remaining mice in this cohort as they are now between 413 and 599 days old.
7. Reported by (name)	Simon Richardson
8. Date	15/6722

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above. There is no obvious cause of death, and although this animal was old, it was not at the two year limit on this protocol. There were no observed pre mortem signs, such weight loss, so this death should be classed as unexplained. I note the intent to cull the cohort. This SC18 can be considered closed.
Inspector name	Neil Smith
Date	1 Aug 22