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	7
Protocol title	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	19/6/22
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	We are studying how mutations in Crebbp and KRas cooperate in the development of B cell acute lymphoblastic leukaemia. We have developed genetically engineered mouse models harbouring these mutations that develop B-ALL. We have flow sorted malignant proB cells from these mice and have transplanted them into immunosuppressed NSG recipients aiming to: 1) formally demonstrate transformation by secondary engraftment and 2) expand material for downstream analysis. The mice undergo sublethal (2Gy) irradiation followed by intravenous injection of donor cells. Mice are weighed regularly and bled from 2 weeks post-transplant. Previous experience transplanting cells of this genotype show a disease latency of approximately 6 weeks. In this case mouse HUAS 42.1a was found dead on 19th June (day 12 following cell return). It had been reviewed daily during the week by our group with no concerns noted and on Saturday 18th by the animal technicians. Its weight had been measured four times in the first week and again on 15th June as per schedule with no significant weight loss noted (15th June 34.7g -0.6% of max). We had not yet bled the mouse as it was typically too early to see engraftment. 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?	In this instance, we did not think advise was required before submitting this report. We do not think that the cause of death is related to the study/experimental procedures and will await the results from the peripheral blood analyses from the other recipient animals before discussing with the vet.

5. Cause of Problem, if known	A post mortem has been conducted. Tissues were decomposed and unsuitable for histology. There was no splenomegaly or other evidence of tumour engraftment, consistent with the early time after transplantation. Cells from this donor have been engrafted into 3 other mice that remain healthy with stable weight. Cells from this sort have been grown in culture with no signs of infection. Given the immunosuppressed nature of the NSG host and lack of evidence of engraftment at this early timepoint, we speculate this may be due to opportunistic infection.
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 continue to monitor the remaining recipients for any signs of discomfort, disease (or infection). We will bleed the remaining three mice in this batch imminently to look for signs of disease engraftment.
7. Reported by (name)	Alicia Garcia-Gimenez
8. Date	21/6/22

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

Inspector's comments and recommendations:

Comments and recommendations	Have read and noted the above. As per 221557, infection due to reduced immune status is plausible. You should discuss with your NVS. This SC18 can be considered closed.
Inspector name	Neil Smith
Date	18 Jul 22