



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	20/6/22
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	We have identified possible new treatments for use in childhood B acute lymphoblastic leukaemia. In order to demonstrate efficacy and tolerability of these therapies in vivo, we are generating a panel of patient derived xenografts for use in future in vivo dosing studies. The mice undergo sublethal (2Gy) irradiation followed by intravenous injection of donor cells. Disease engraftment and dissemination is typically monitored by means of flow cytometry of peripheral blood (routinely sampled starting from 2 weeks post transplantation). Our experience with these PDX derivation systems, is that engraftment typically takes many months (>2months post transplantation). In this case mouse HUAS 35.1f was found dead on 20th June, day 6 following intravenous injection of patient derived leukaemia cells. 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 and over the weekend of 18-19th June by the animal technicians. Its weight had been measured three times since irradiation as per schedule with minimal weight loss noted (15th June 31.8g -2.2% of baseline). We had not yet bled the mouse as it would have been 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?	We believe we have a probable explanation for this animal's death, and we are planning on discussing the prophylactic use of antibiotics with the NACWO and named Vet, in order to potentially minimise the incidence of opportunistic infections post transplantation.

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 engraftment (e.g. lymphadenopathy), an obligate phenotype of our PDX system. This was consistent with the early time after transplantation. 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 an 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 discuss with the NACWOs regarding the use of prophylactic antibiotics in transplants involving irretrievable patient-derived material.
7. Reported by (name)	Simon Richardson
8. Date	21/6/22

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	