



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 (Huntly) Investigation of normal haematopoietic stem cell subversion and the evolution, maintenance and targeting of haematological malignancies
Protocol no	7
Protocol title	[Moderate] 07 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	16/03/22
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	A mouse on the study plan SP126461 was found dead on 16/03/22. Animals on this study are used as primary recipients to assess the engraftment potential of a malignant population generated from a previous mouse model. This animal was lethally irradiated on 07/03/22 and injected with malignant cells mixed with healthy helper bone marrow cells. The mouse was then monitored daily, weight was recorded and mash diet was given as specified in the study. Although the mouse did not show weight loss in the early days post-irradiation, a weight loss of 11% was noticed on 14/03/22. The mouse was given mash diet, was checked and weighed daily thereafter. Weight loss had increased to 13% on 15/03/22. Weight loss is common after irradiation and it was still within the limit authorised in the study. No clinical signs were seen on daily checks that would have indicated discomfort or disease. The necropsy revealed that a section of the intestine was surrounded by adherent tissue. We speculate that this could have created a blockage that prevented the mouse to feed properly resulting in loss weight. All other tissues looked normal. Tissues were processed for cytometry analysis and samples will be sent to histology for analysis.
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. However, the necropsy suggests that the mouse may have had issues to feed itself, explaining the weight loss. The death seems unrelated to the study.

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>	Tissues have been processed for downstream analysis by flow cytometry. Tissues have also been put into Formalin and will be sent for analysis. We speculate the death was not related to the study and possibly due to the abnormality in the intestine.
7. Reported by (name)	Nathalie Sakakini/Ryan Asby
8. Date	18/03/21

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

Inspector's comments and recommendations:

Comments and recommendations	• Thank you for this SC18 report. • Death is considered to be a severe severity classification and as protocol 7 is denoted of moderate severity there has been a breach of protocol severity, triggering a SC18 report. • Your actions and proposals in response to this incident are appropriate and welcomed. • I consider this case closed. • However, please note that advice should ALWAYS be sought from the NACWO/NVS for incidents requiring the completion of a SC18 Report and their advice should be listed – even if it is to continue as you have been doing. • I find it unlikely that this incident was caused by an abnormality of the intestine that was <u>not</u> procedure related when irradiation is well known to affect this organ so significantly. Sometimes you can do everything correctly and things still go wrong, this is what SC18 Reports are for.
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Inspector name	Mark Dagleish BVM&S, PhD, MRCVS, FRCPath
Date	24 th March 2022

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