Home Office

210246

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	University of Cambridge, The Anne Mclaren Building
Establishment Licence number	X81BD37B1
Name of PPL holder	Brian Huntly
PPL number	PP3042348
Protocol no	07

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	14/08/2021
2. Species	Mouse

3. Brief details of study and how the limits or constraints have been breached	The study involves generation of haematopoietic chimaeras using highly purified human haematopoietic stem cells. One mouse was found dead by AMB staff without having shown any previous signs of disease or discomfort. Mice on this study are visually inspected by members of our team or AMB staff at least once a day for signs of ill health including lack of mobility and hunched backs. After irradiation mice are weighed twice weekly by members of AMB staff until weight returns to pre-irradiation weight. No significant weight loss had been recorded for this animal. The reference weight at the time of irradiation (1/06/2021) was 29g and the weight at the last weighing time point (14/06/2021) was 29.1g. The proportion of mice that have been found dead after performing the same regulated procedures in the hands of our group is very low (4/1064 mice and therefore 0.4%). This animal had received a sub-lethal dose of irradiation, followed by IF injection of cells on the 2nd June 2021. The time of death (>7 weeks after irradiation) excludes any complications from irradiation. On the 28th June 2021, the mouse was bled via tail vein and noted on the monitoring sheet to be alert with no obvious side effects after the procedure. The lack of human cells in the blood sample taken suggests that this is not an effect of the human HSCs injected on 2nd June 2021. The mouse was found dead during morning checks on 14/8/21 by Andrew Cavil, an AMB technician. The mouse was last checked by AMB staff Friday evening (13/8/21) but no report of ill health was reported. No necropsy was performed as the animal was found dead on a Saturday and the mouse was not stored by the technician for tissue studies (although the study plan states to keep any mice for tissues).

4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Yes. We have spoken to the staff in the Cat2 room. They had not noticed anything unusual.
5. Cause of Problem, if known	Unknown
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 inspect these animals (along with AMB staff) at regular intervals. In the unlikely case this was to occur again, we will make sure that tissues are sent to the veterinary. Mice will now be weighed once a week on the study plan to have comparison weights in case of ill health
7. Reported by (name)	Emily Calderbank
8. Date	16/08/21

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

Inspector's comments and recommendations:

Comments and recommendations	Dear Emily Thank you for submitting this PPL Standard Condition 18 notification reporting that a mouse was found dead on 14/08/2021. The severity classification of protocol 7 is moderate and therefore there has been a breach of protocol severity, triggering a SC18 report. Further information is required: The information currently given on monitoring is rather vague: '*Mice on this study are visually inspected by members of our team on a regular basis and after irradiation are weighed twice weekly by members of AMB staff'.* Please provide more detailed information (dates of observations/ examinations) on the monitoring regime that was implemented by the relevant PILh(s) responsible for the experiment. What was the date and time of last observation prior to the mouse being found dead? At what time was the mouse found dead on 14 August, and by whom? The report states that the mouse died on 14/08/2021 having commenced on procedure on 01/06/2021 (approximately 10.5 weeks). The reports states: • *'The weight at the last weighing time point (14/06/2021) was 29.1g'* • *'On the 28th June 2021, the mouse was bled via tail vein and noted to be alert with no obvious side effects after the procedure'*. Why was the last weighing on 14/06/2021 when there was a commitment to weigh twice weekly? The report states that: '*No significant weight loss had been recorded for this animal'*. This does not really support the implication that the mouse was in reasonable health until around the time of its death, which was not until over two months later; please clarify. It is expected that advice would be taken from named persons, particularly the NVS, when serious adverse effects occur (as here) to try to ascertain cause of the death /adverse effects, and to review the experiment to make appropriate changes to prevent recurrence of the problem in future. The report states: '*Yes. We have spoken to the staff in charge of the Cat2 room. They had not noticed anything unusual'*. The report gives no indication as to whether NVS advice was sought on likely cause of death or on preventative/ safeguarding (e.g. review of

	monitoring regime) measures for future experiments. Has this been done? **Please note** that any additional information should be returned on this report form by adding to the information that is already present in a colour other than black e.g. red to make the additional information clear to the reviewing Inspector. *Dear Emily* *Thank you for the additional information and revised report. Please note that it is expected that advice would be taken from named persons, particularly the NVS, when serious adverse effects occur (as here) to try to ascertain cause of the death /adverse effects, and to review the experiment to make appropriate changes to prevent recurrence of the problem in future.* *I now consider the matter closed.* *Please continue to report any further issues that may occur.* *Karen Mason* *31/08/2021*
Inspector name	Karen Mason
Date	17 August 2021