232412 – FD/AE

Home Office

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 (Huntly) Investigation of normal haematopietic stem cell subversion and the evolution, maintenance and targeting of haematological malignancies
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	30/10/2023
2. Species	Mouse
3. Brief details of study and how the limits or constraints have been breached	The specific study uses a murine leukaemia cell line that gives rise to leukaemic transformation with a 100% penetrance. As such, mice under this study plan had received a lethal dose of irradiation (on the 4th of October 2023) followed by intravenous injection of murine cells. The study was comprised of 10 mice. One mouse on study plan SP138033 was found dead on Monday 30th of October 2023.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	No advice was requested as preliminary results were highly suggestive of leukaemia. The NACWO will be cc'ed on the correspondence of this report.
5. Cause of Problem, if known	Leukaemic disease progression (acute and of sudden onset). Macroscopic examination of the animal demonstrated splenomegaly, (an obligate phenotype for this model system). This animal had been visually inspected on the previous day(s) by the AMB staff and a member of our team and displayed no clinical symptoms. Multiple animals on this study plan went on to display clinical symptoms consistent with moderate severity and our expected phenotype. Analysis of the tissues (flow cytometry analysis of BM and spleen tissue) obtained has confirmed leukaemic disease progression.
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)*	The remaining animals in this cohort were thoroughly inspected for any signs of distress or ill health (including weighting and a scheduled blood sample). Within 24hours five additional animals went on to display clinical symptoms consistent with moderate severity and were sacrificed. The remaining animals are still under close observation and additional blood sampling has been scheduled one week from today.
7. Reported by (name)	George Giotopoulos

8. Date	01/11/2023

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

Inspector's comments and recommendations:

Comments and recommendations	Thank you for submitting this PPL SC18 Notification. Further information is required as described below: • Details of the lethal irradiation: what total dose was administered, was this given in split doses and was it administered as whole body or hemi /partial body • The records of body weight of each of the mice on the study • The report states that within 24 hours five additional animals went on to display clinical symptoms consistent with moderate severity. Describe the clinical signs that were observed. • The implication from this report is that in this study 6/10 mice did not survive until the intended scientific endpoint. What changes do you intend to make to the design of future studies to try to ensure that you can achieve your scientific objectives? Have you taken advice from the NVS, NACWO in this regard? **Please note** that any additional information should be returned in the form by responding to this email and adding **the report ID** to the email subject to assist with onward processing.
Inspector name	Karen Mason
Date	28/12/2023