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	Rachel Watson
PPL number	PP6298217
Protocol no	03a
Protocol title	Investigation of the pharmacokinetics of test agents (non-instrumented) (Mice)
Severity classification	Mild
1. Date of incident	20th March 2025

2. Species	Mouse – C57BL/6J
3. Brief details of study and how the limits or constraints have been breached	The aim of this study was the investigation of the pharmacokinetics of a single oral dose of Leucettinib-21. Leucettinib-21 is a pharmacological inhibitor of dual-specificity, tyrosine, phosphorylation-regulated kinase 1A. Leucettinib-21 was administered via the oral (p.o.) route at a dose of either 3 or 30 mg/kg in a volume of 10 ml/kg. Dosing was staggered to allow for observation of any acute clinical signs in the first mice dosed prior to dosing the subsequent animals in each group and ascending in dose. No clinical signs were observed in this period with either 3 or 30 mg/kg Leucettinib-21. Mouse 6 (dosed with 30 mg/kg Leucettinib-21), started to show clinical signs of lethargy, hunched posture and a continuous piloerect coat following collection of a blood sample 6 hours post dosing. As no clinical signs that are greater than mild or transient are expected on this protocol the mouse was immediately culled and necropsy performed. At necropsy it was noted that the liver was pale and the right axillary lymph node region had a brown and white discharge under the right forearm. These tissues were collected for histological evaluation. No mice treated with 3 mg/kg Leucettinib-21 displayed any clinical signs and the remaining 2 mice treated with 30 mg/kg Leucettinib-21 did not display any clinical signs up to the terminal time point of 24 hours post dose. Tissues from all the remaining animals appeared normal at necropsy.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Due to the time at which the animal was observed with clinical signs and the fact that these were clearly not within those included in the PPL action was immediately taken and the NACWO or Vet was not called for advice prior to Schedule 1. The NACWO has been informed of the issue prior to submission of the SC18.

5. Cause of Problem, if known	The cause of the problem is not fully understood. The absence of clinical signs or abnormal tissues in the other animals treated with the same concentration suggests it is not related to toxicity of Leucettinib-21.
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 the study were closely monitored for the remainder of the time on study. The abnormal tissues collected from Mouse 6 will be histologically examined to attempt to ascertain the cause of the clinical signs observed.
7. Reported by (name)	Rachel Watson
8. Date	

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	