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 (Mira)
Establishment Licence number	X81BD37B1
Name of PPL holder	Rachel Watson
PPL number	PP6298217
Protocol no	3
Protocol title	Investigation of the pharmacokinetics of test agents (non-instrumented)
Severity classification	Mild
1. Date of incident	05/10/2023

2. Species	Rat
3. Brief details of study and how the limits or constraints have been breached	As stated in section 6 of the SC18 report submitted on 04/10/2023, to investigate unexpected toxicity observed in rats when dosing 2 compounds intravenously, that had previously been dosed intraperitoneally in mice without adverse effects, a single rat was dosed with the vehicle formulation (5% DMSO, 40 % Transcutol, in beta cyclodextrin) observing effects of vehicle dosing alone. The animal was warmed in a heating cabinet set at 38°C for 10 minutes, placed into a restrainer and dosed with the vehicle formulation at 5ml/kg as per the procedure for the injections carried out on 04/10/2023. Unfortunately, a similar reaction was observed to the compound dosing, with the animal requiring resuscitation immediately after being removed from the restrainer. Following successful resuscitation, the animal was displaying laboured breathing and appeared to be subdued so the decision was immediately taken to cull the animal.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	The NVS and NACWO were aware that this was being undertaken to investigate the toxicity previously observed.
5. Cause of Problem, if known	This has given a clear indication that this combination of excipients (5% DMSO, 40 % Transcutol, in beta cyclodextrin) is not tolerated by rats when delivered intravenously.
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)*	No further intravenous dosing will be undertaken with this vehicle formulation in rats.
7. Reported by (name)	Rachel Watson

8. Date	05/10/2023

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	