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.**

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| **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** | 12/10/2022 |

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| **2. Species** | Rat |
| **3. Brief details of study and how the limits or constraints have been breached** | The aim of this study is to test new formulations of a novel compound for improved exposure, prior to use in the rat Sugen-hypoxia model of pulmonary arterial hypertension. In this study, the new formulation is administered in wild-type rats, and blood collected for subsequent pharmacokinetic analysis.<br><br>On 12/10/2022 two members of our team were taking baseline blood samples the day before the PK was due to start, i.e. before any test agent dosing took place. One team member was training in blood sampling from a superficial vessel (Yateen Patel) and was being trained/observed by another (Michael Penn). Rats were put into a standard commercially available restrainer (VetTech), and blood was sampled from the tail vein. This was not the first time the trainee had performed the procedure, previous training had been successful. Baseline blood sampling was timed at 5 minutes between each animal, in order to simulate for timed bleeds similar to that in a PK, but with longer gaps (usually 2.5-3 minutes).<br><br>Blood sampling from the first 10 rats in the cohort were conducted by the trainee with no problems. The 11$^{th}$ rat to be bled (M00898125) was put into the restrainer as normal, and the tail vein puncture was done. Blood didn't flow from this attempt, so another was made (all within three minutes of the rat going into the restrainer). When blood didn't flow on this attempt, the trainer told the trainee to remove the rat from the restrainer.<br>Upon removal the rat was found dead; both trainee and trainer attempted to resuscitate animal without success.<br><br>Subsequent animals in the cohort were all monitored more closely while blood sampling. Another animal, also in the correct restrainer position, became slightly limp, which was noticed by trainer/trainee and was immediately removed. This animal recovered within seconds and further monitoring showed no clinical signs. |

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| **4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?** | NACWO and NVS have been notified and advice sought on any contributing factors. |
| **5. Cause of Problem, if known** | On post-mortem the rat was found to have an extremely distended GI tract, with air/gut contents from stomach to caecum, and proximal colon full of gut contents. This distension was extensive, so could have caused breathing difficulties while being restrained.<br><br>No other abnormalities were seen; heart, lungs and spleen appeared normal.<br><br>Trainee conducted the procedure correctly, however the animal was in the restrainer for 3.5 minutes; although it is unclear whether this contributed, it was longer than normally taken when fully trained. |
| **6. Action that has been or will be taken**<br>*(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)* | Trainee will continue to be trained under close supervision until trainers assess him to be fully competent; this includes becoming quicker at taking the sample.<br><br>Although the restrainer is commercially bought and has not caused issues previously, we are going to modify the nose cone. On suggestion of the trainer who has done it previously, we will drill multiple small holes into it, which may help to allow for more air to circulate through the restrainer. |
| **7. Reported by (name)** | Yateen Patel and Amy Warner (on behalf of Rachel Watson). |
| **8. Date** | 13/10/2022 |

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

## Inspector's comments and recommendations:

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| **Comments and recommendations** | |
| **Inspector name** | |
| **Date** | |