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	Elisa Galliano
PPL number	PP0165908
Protocol no	8
Protocol title	Neonatal/adult injection, with/without electroporation, with optional modulation of neuronal activity
Severity classification	Moderate
1. Date of incident	25.01.2024
2. Species	Mouse

3. Brief details of study and how the limits or constraints have been breached	The study entailed stereotaxic injections in the brain to express a modulator of neuronal activity in specific brain cells. Given the issues encountered last month with the anaesthetic, we used a clean wild-type mouse to remove the genetic background variable. The experimenter has extensive experience in this type of surgery from their previous work, they competed the mandatory PIL A-C training, and they have received full training for this specific facility (induction and shadowing of other experienced users). The location of the target brain area (olfactory bulb) is very close to the nose, so the procedure was performed using injectable anaesthesia (ketamine and xylazine) instead of inhalation anaesthesia (isoflurane). This is to maintain sterility around the incision while properly accessing the brain. Given the problems with overdoses that we had last month, as per NVS suggestion the animal was induced by a senior surgery technician with 80% standard volume of a ketamine/xylazine dose. The induction was smooth, but it required two top-ups to complete the surgery, which went well. The animal took a couple of hours to wake up, and the experimenter stayed with it the entire time to monitor its breathing, which was normal. When it was clearly awake and mobile (crawling, whisking etc.) the experimenter moved it to a single housed cage with postoperative gel mash. The animal was found dead the following morning. The vet performed a postmortem, and the experimenter collected the brain to try and use the tissue.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Given the controlled substance status of ketamine, and the issues that we had previously with overdose, the NVS and a senior surgery technician were present for the entire duration of the procedure. They advised on the dosages using the lower range of the standard recommended figures, and assisted the experimenter throughout. They commented on the fact that the experimenter performed all steps exemplarily.
5. Cause of Problem, if known	The animal was a C57Bl6 imported from Charles River earlier in the year. The NVS performed a postmortem on it, and found large quantities of bile in its digestive tract. It is unclear if that caused the death, but it is a possibility.

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)*	As per NVS advice, we will (a) order new wild type mice; (b) use a slightly higher dose to induce (85%-90%) to try and avoid a second top up; (c) if a second top up is necessary, do it only with ketamine (xylazine has a longer half-life); (d) have the xylazine reversal agent ready to use if the animal takes a long time to wake up; (e) keep on performing all procedures with the NVS present for support until we have pinpointed a stable anaesthetic regime and we have a couple successful surgeries.
7. Reported by (name)	Elisa Galliano
8. Date	15.02.2024

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

Inspector's comments and recommendations:

Comments and recommendations	
Inspector name	
Date	