



# 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.

|                                     |                                                                                  |
|-------------------------------------|----------------------------------------------------------------------------------|
| <b>Establishment Licence name</b>   | University of Cambridge                                                          |
| <b>Establishment Licence number</b> | X81BD37B1                                                                        |
| <b>Name of PPL holder</b>           | Maria P. Alcolea                                                                 |
| <b>PPL number</b>                   | PP7037913                                                                        |
| <b>Protocol no</b>                  | 07                                                                               |
| <b>Protocol title</b>               | <b>Changes in epithelial cell behaviour in response to tissue perturbations.</b> |
| <b>Severity classification</b>      | Moderate                                                                         |
| <b>1. Date of incident</b>          | 15.07.2025                                                                       |
| <b>2. Species</b>                   | Mus musculus                                                                     |

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| <p><b>3. Brief details of study and how the limits or constraints have been breached</b></p> | <p>Gene induction with Tamoxifen.</p> <p>This study plan SP147844 (MA_DR_009_RosaCre RosaConfetti DEN) includes 17 animals bearing the confetti cassette that is conditionally expressed upon tamoxifen injection, mediated by the Cre<sup>ERT</sup> activity. The cassette expression and Cre are harmless to the animal, but mice treated with Tamoxifen or other gene induction agents might show weight loss.</p> <p>The animals were injected on Sunday Morning (13<sup>th</sup> of July) subcutaneously with tamoxifen 5mg/20g dose on the nape area. Weight was monitored and visual assessment post-injection performed. The animals were also weighed and injected on Monday Morning (14<sup>th</sup> July) according to the study plan. No animal showed any sign of distress or significant loss of weight at the time of the second injection. As part of the refinement procedure, and after previous revision of the procedure together with the NVS, the second injections were performed on the flank of the animals.</p> <p>The animals MADP4.1g and MADP4.1h were found dead on Tuesday morning during the routine technician check. During the day on Monday the animals were also checked by the technicians as part of the routine checks. The injection technique was previously monitored by the NVS Sophie Kimpton to ensure that the user (Davide Rossetti, Licence I72161586) could correctly perform the procedure on the named anatomical sites. In this study plan, the max dose of 5mg/20g Tam was used. It is expected that the animals did not tolerate the drug as it can happens in low rates across different strains. The other animals in the study are being monitored. Autopsy of the animals reported slightly enlarged liver and stomach.</p> |
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| <b>4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?</b>                                                                                                                                                               | <p>The weighing regime has been discussed previously with Polly to ensure the animals are monitored in the best way and we hope that this will be possible to continue.</p> <p>The NVS was previously consulted to design a strategy minimising the animals distress and symptoms from the administration of Tamoxifen at high doses.</p>                                                                                                                                    |
| <b>5. Cause of Problem, if known</b>                                                                                                                                                                                                                                          | <p>Drug toxicity</p> <p>NVS inspected the animals post-mortem and found enlarged liver and stomach, possibly in coherence with tamoxifen toxicity. No evidence of incorrect dosage could be found or injuries related to incorrect injection. Organs were sent for histopathological analysis.</p> <p>Some of the other animals in the study plan, that received the same dosage, have experienced weight loss to various degrees, as expected from tamoxifen injection.</p> |
| <b>6. Action that has been or will be taken</b><br><i>(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)</i> | <p>Close monitoring in the near future will allow the early poor health identification and the humane end points will take action. Adding more frequent visual checks on animals of concern is vital and the animals in this group will be closely monitored and provided with appropriate support. We will also consider using the moderate dose of 3mg/20g instead.</p>                                                                                                    |
| <b>7. Reported by (name)</b>                                                                                                                                                                                                                                                  | Davide Rossetti, animals found by Lucy Haslam                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>8. Date</b>                                                                                                                                                                                                                                                                | 16/07/2025                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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

**Inspector's comments and recommendations:**

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|-------------------------------------|--|
| <b>Comments and recommendations</b> |  |
| <b>Inspector name</b>               |  |
| <b>Date</b>                         |  |