



# 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]

|                                     |                                                         |
|-------------------------------------|---------------------------------------------------------|
| <b>Establishment Licence name</b>   | University of Cambridge                                 |
| <b>Establishment Licence number</b> | X81BD37B1                                               |
| <b>Name of PPL holder</b>           | Prof Stefan Marciniak                                   |
| <b>PPL number</b>                   | PP5789170                                               |
| <b>Protocol no</b>                  | 4                                                       |
| <b>Protocol title</b>               | Breeding and maintenance of genetically altered animals |
| <b>Severity classification</b>      | Mild                                                    |
| <b>1. Date of incident</b>          | 11/4/2023                                               |
| <b>2. Species</b>                   | Mouse                                                   |

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>3. Brief details of study and how the limits or constraints have been breached</b>                                                                                                                                                                                         | During the normal breeding to maintain a double knockout colony a female mouse (MKAC4.3f) with a 4 day old litter was found dead with rigor mortis on the morning of the 11 <sup>th</sup> April 2023 by the animal technicians. MKAC4.3f had no obvious injuries. The technician then moved the litter to another female (MKAC7.1f) with a 1 day old litter. MKAC7.1f was observed to be healthy and moving the new pups around. Approximately 10 minutes after placing this cage back on the rack MKAC7.1f was found dead. This mouse was then cervically dislocated and left in the fridge for postmortem. All pups appeared healthy and were sch1 due to no alternative fosterer. |
| <b>4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?</b>                                                                                                                                                               | We have taken the advice from the NACWO to monitor if this problem persists. It has not been reported in the literature before that mice with these mutations have this problem. As far as we are aware no-one else has bred this specific double mutant mouse.                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>5. Cause of Problem, if known</b>                                                                                                                                                                                                                                          | I dissected both MKAC4.3f and MKAC7.1f and found both had significant blood clots in their peritoneal cavities. It is possible this was the primary cause of death. Nothing else out of the ordinary was noted. MKAC4.3f was heterozygous for mutations in the gene IL6 and MKAC7.1f was homozygous for mutations in IL6 and heterozygous for mutations in GCN2. We have been breeding mice with mutations in both IL6 and GCN2 for 10 months and have not encountered this problem before.                                                                                                                                                                                          |
| <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> | We will continue to check if this problem persists or if there is any unusual peritoneal bleeding in the mice in this line. If the problem does persist, we will refresh the line by introducing a new wildtype mouse.                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>7. Reported by (name)</b>                                                                                                                                                                                                                                                  | Max Schwiening                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>8. Date</b>                                                                                                                                                                                                                                                                | 11/04/2023                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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

**Inspector's comments and recommendations:**

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

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