ID 241322_FD-S

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<br>Combined Animal Facility, Department of PDN |
| **Establishment Licence number** | X81BD37B1 |
| **Name of PPL holder** | Ole Paulsen |
| **PPL number** | PP0499088 |
| **Protocol no** | 09 |
| **Protocol title** | Circuit mechanisms of learning and memory in the mammalian brain |
| **Severity classification** | Moderate |
| **1. Date of incident** | 19/06/2024 – 25/06/2024 |

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| **2. Species** | Mouse |
| **3. Brief details of study and how the limits or constraints have been breached** | Seven pups underwent intracranial AAV injection at P3. The aim of the study is to express WT and mutant forms of GluN1, the NMDA receptor subunit, in GluN1 KO animals so that mechanisms of NMDA receptor signalling can be investigated. In this case, the injected AAV encoded the wild type subunit.<br><br>These AAV injections are done between P1 and P6 in pups, so that the GluN1 subunits will be expressed in functional NMDA receptors by P14 when brain slices are prepared and recordings are made. This is the first time that this particular virus has been used, but the procedure has been successfully carried out by the same operator in several previous litters with other AAVs.<br><br>The pups were observed carefully throughout the procedure and during a post-operative recovery period. One pup did not recover from the isoflurane anaesthetic. The remaining six pups were seen to recover well and were observed to be accepted by the mother when returned to their home cage and in the days following.<br><br>No ill health of the pups was reported to PIL holder who performed the procedure or the PIL holder who manages the mouse line prior to the pups being found dead on 19/6/24, 20/6/24, 21/6/24, 22/6/24, 24/6/24, 25,6/24.<br><br>The animal facility has had issues with murine hepatitis virus (MHV) affecting breeding and there have been several instances of total litter losses before P5 in lines of other genetic backgrounds with no procedures having been administered. It is not clear in this instance whether it is the procedure given that these animals were older at death or another unrelated cause which led to their premature deaths. |
| **4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?** | The incident has been reported to NACWO and will be discussed further. |

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| **5. Cause of Problem, if known** | Cause of problem is unknown. It is difficult to know whether the cause is related to the procedure. |
| **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)* | More regular checks on pups post-procedure will be discussed with the lab technicians. Moving forwards, AAV injections will be carried out in a different facility which has had fewer issues with breeding. |
| **7. Reported by (name)** | Matthew Roxby<br>PPL holder (Ole Paulsen) is informed. |
| **8. Date** | 08/07/2024 |

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

## Inspector's comments and recommendations:

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| **Comments and recommendations** | Thank you for submitting this notification and thereby complying with standard condition 18 of your project licence (unexpected deaths).<br><br>Further information is required as described below:<br><br>-please provide the outcome of discussing this situation with the NVS, and what steps they advise<br><br>-please advise whether there have been other circumstances relating to AAV injection of pups **within last 6 months** that led to adverse outcomes such as found dead or pups that you needed to cull due to clinical signs/reaching humane endpoint unexpectedly. Please provide summary table as appropriate.<br><br>-You have indicated that there may be an underlying MHV issue in the unit concerned please provide further detail of the measures that are being taken to further investigate/address this issue.<br><br>**Please add** this additional information to this form and return it by email by 26th July 2024.Remember to quote the notification's **ID number** in the email subject, to assist with onward processing. (ID241322_FD)<br><br>Thank you for providing the requested information. I have reviewed our response and this matter is now CLOSED. |
| **Inspector name** | Nicola Watts |
| **Date** | 17/07/24 30/07/24 |