



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]

Establishment Licence name	University of Cambridge
Establishment Licence number	X81BD37B1
Name of PPL holder	Maria P. Alcolea
PPL number	PP7037913
Protocol no	7
Protocol title	Changes in epithelial cell behaviour in response to tissue perturbations
Severity classification	Severe Moderate

1. Date of incident	Thursday 19th May 2022
2. Species	Mouse (M00534816)

3. Brief details of study and how the limits or constraints have been breached	This study plan (SP078271, MA_EJH_002_06) includes in total 15 animals that are receiving low doses (40mg/L) of DEN carcinogen via drinking water for 2 months. On the 15th February 2021 the M00534816 animal started DEN carcinogen treatment and received 28 low doses out of 28 via drinking water prior to death. The animal did not show any signs of drastic weight loss and so did not have any health concerns as the animal was healthy and the weight loss did not breach 10%. If animal reaches 10% weight loss the technicians notify user for health concern. Animals are not expected to show any adverse clinical signs as a result of DEN treatment, except for weight loss and incidental tumours such as lipomas as they age. Sporadic liver damage was occasionally observed resulting in early animal collection and is a potential reason for this animal being found dead. Animals receiving DEN or after DEN treatment are monitored by weighing daily for the first week, weekly for the next month and then once every two months. Animals are also checked every day for any clinical signs or abnormal behaviour as done by the facility technicians on a daily basis. Any concerning animals go back to weighing every other day or daily, if necessary, until the weight is stable again. If the concerning signs do not resolve within 24 hours they are culled. In the event of worsening clinical signs animals will be immediately culled. If vital processes such as eating, defecating and breathing are compromised, as identified in regular inspections, animals are culled immediately. Any animal showing weight loss of 10% will be moved to a mash diet and any weight loss of 15% or more for 2 consecutive days are to be culled immediately. Animals receiving DEN or after DEN treatment are monitored by weighing daily for the first week, weekly for the next month and then once every two months. Animals are also checked every day for any clinical signs or abnormal behaviour.
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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. 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. The animal was not reported as being sick earlier this week. The incidence of sudden death during DEN treatment has been observed before as a rare event, we believe all actions to accommodate any changes in animal health are already in place.
5. Cause of Problem, if known	M00534816 had a very swollen abdomen, was moving slowly, displaying a moderate hunch and had laboured breathing, therefore the animal was culled immediately on welfare grounds . Upon dissection, fluid was found to be collected in her abdomen, and the spleen and liver were very enlarged. The liver was also mottled and covered in cysts. The animal likely died from liver failure due to an adverse reaction to DEN carcinogen.
6. Action that has been or will be taken	The animal did not show any signs of drastic weight loss (0% from baseline), which did not cause any health concerns as the animal was healthy. In addition, none of the other 15 animals receiving the same batch of drug showed any signs of concerning health.
7. Reported by (name)	Emily Jane Hill, animal found by Rebecca Douthwaite
8. Date	19/05/2022

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

Inspector's comments and recommendations:

Comments and recommendations	• Thank you for this SC18 report. • Death is considered to be a severe severity classification and as protocol 7 is denoted of moderate severity there has been a breach of protocol severity, triggering a SC18 report. • Further information is required as described below: — The box on the first page of this report requesting the severity is that as listed in the protocol – not that experienced by the animal(s). — You state this animal 'M00534816 had a very swollen abdomen, was moving slowly, displaying a moderate hunch and had laboured breathing' and you project licence states 'If animals show any clinical signs such as hunched posture, piloerection or subdued behaviour, these animals will kept under close observation. If the signs do not resolve within 24 hours they will be killed. In the event of worsening clinical signs animals will be immediately killed'. So, why was this animal not killed as it had obviously reached, and probably exceeded while still alive, the humane endpoint in the project licence? — Please note that any additional information <u>should be returned on this initial report form</u> by adding to the information that is already present in a colour <u>other than black</u>, e.g. red, to make the additional information clear. — Please also add the case number 221176 to the header of your return Email to assist with onward processing.
Inspector name	Mark Dagleish BVM&S, PhD, MRCVS, FRCPath
Date	27 th May 2022