



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 Anne McLaren Building
Establishment Licence number	X81BD37B1
Name of PPL holder	Menna Clatworthy
PPL number	PD030666A
Protocol no	8
Protocol title	Infection or inoculation with pathogen or pathogen-derived molecule
Severity classification	Moderate
1. Date of incident	12/11/2023

2. Species	Mus musculus
3. Brief details of study and how the limits or constraints have been breached	The study aims at IP injecting PBS control, ovalbumin, and heat-killed bacteria that expresses ovalbumin or its fragments to study if OVA-specific B cell and T cell responses can be generated. As a pilot experiment, only 2 mice were used for each cohort, and bacteria (<i>E. coli</i> and <i>Salmonella</i>) were heat-killed at 70 degrees Celsius for at least 20 minutes. In protocol 8, the humane endpoint is up to 15% weight loss compared to pre-experimental weight, and they will also be humanely killed if the mice show up to three of the following signs: 1) Piloerection, 2) Lethargy, 3) Abnormal rapid breathing, 4) Diarrhoea, and 5) Dehydration. Two mice (in the same cohorts with heat-killed <i>E. coli</i>) were found dead in the next morning, and four mice (two other cohorts) losing between 7 to 10% of weight and showing lethargy and dehydration. 3 of the 4 mice were culled humanely after consulting with the NACWOs.
4. Have you taken advice from the Named Animal Care and Welfare Officer/Named Veterinary Surgeon/others?	Yes, the NACWOs recommended to cull the mice when the live mice reached close to 10% weight loss, and the animals were culled. One animal had much better situation as it was housed with 4 other animals in better conditions, so it was kept for another day. However, it continued to lose weight, so with the NACWOs advice, the last mouse was culled at 14% weight loss, just below 15% weight loss as the upper limit.
5. Cause of Problem, if known	Post mortem biopsies were performed, and no clear abnormalities were noticed by examining the peritoneal cavity, the intestinal tract, the liver, the kidney, and the spleen. Two other experimental cohorts remained completely fine after the IP injection, so it is unlikely that the IP injection was performed incorrectly. The heat-killed bacteria at large amount together with freshly prepared aluminium hydroxide might have caused too strong of an immune response. For instance, the cohorts that found dead were injected heat-killed <i>E. coli</i> that expresses the OT-I peptide, which potentially caused a very strong response.

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)	The study design will be modified. The IP injection experiment may not be the best approach. I will instead administer live bacteria via oral gavage. This study will most likely not be repeated.
7. Reported by (name)	Qianchang (Dennis) Wang
8. Date	15/11/2023

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

Inspector's comments and recommendations:

Comments and recommendations	Thank you for submitting this notification and thereby complying with standard condition 18 of your project licence. The content of this SC18 report has been read by an ASRU Inspector and this matter is now CLOSED. Please continue to inform us of any other similar incidents should they occur.
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