

Lawrence Livermore National Laboratory

Supplement to USDA Annual Report of Research Facility – Fiscal Year 2021

Registration Number: 93-F-0018 - Customer Number: 1245

Assurance Statements

A summary of all (two) exceptions is provided below. In addition to identifying the IACUC approved exceptions, the summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

The single housing exception was first approved by the IACUC on the new protocol August 20, 2020, and again on the annual renewal August 20, 2021.

97 Guiana pigs were single housed. They were single housed because the animals had jugular vein catheters and needed to be housed singly to avoid damage to the catheters by potential chewing from other animals. Also, the animals were housed in single metabolism cages for 24 hours while on test. Animals were also singly housed to avoid injury while on test.

The exception to use non pharmaceutical grade atropine was first approved by the IACUC on an amendment March 22, 2021.

84 Guiana pigs received non-pharmaceutical grade atropine sulfate.

Amendment request: We are requesting the use of non-pharmaceutical grade atropine sulfate will be substituted for pharmaceutical grade atropine sulfate due to the pharmaceutical grade formulation being extremely hard to acquire at this time. An order was placed for pharma-grade atropine sulfate in Dec 2020 and has been placed on indefinite back order with no timeline for delivery. According to the vendor there is a nationwide shortage of pharmaceutical grade atropine sulfate due to its use to treat COVID-19 patients that develop bradycardia.

The main manufacturer is Pfizer which has shifted their manufacturing priorities to the COVID-19 vaccine. Extensive efforts have been made to locate an alternative distributor/brand. These efforts included working with the primary vendor to identify alternate sources/manufacturers to try and acquire the compound. None of these efforts were successful. To continue the work, we will use non-pharma grade atropine sulfate at the highest purity available. The compound will be dissolved in pharma-grade saline and the purity will be checked by high performance liquid chromatography prior to dosing animals. A purity $\geq 98\%$ will be considered sufficient for exposure to the animals.

As of September 8, 2021, pharmaceutical grade atropine is still unavailable. Pharma-grade atropine sulfate will be used if supplies become available.