TACONIC

January 1, 2013

Dear Investigator,

Taconic Biosciences has been pleased to facilitate the distribution of the SOD1 Mutant Rat (Taconic model 2148) through our Emerging Models Program, wherein model Sponsors maintain colonies at Taconic for widespread distribution. The purpose of this communication is to provide an update on phenotypic changes in the SOD1 colony. The SOD1 rat model, developed as part of a collaboration between The ALS Association and Wyeth, has been sponsored at Taconic through grant funds from The ALS Association. This rat model provides an important model of Amyotrophic Lateral Sclerosis, and it has been widely used for research on this disease.

The SOD1 rat model displays a disease phenotype involving motor dysfunction and paralysis. The original publication on this strain, PNAS 2002, 99(3):1604-1609, reported disease onset around 115 days of age, with rapid disease progression thereafter. Taconic has maintained a colony since 2002, with production via mating hemizygous transgenic males to wild type Sprague Dawley females (NTac:SD). Taconic does not routinely hold saleable inventory animals longer than approximately 12 weeks of age, but we do hold male breeders much longer. Taconic has tracked onset of disease symptoms such as abnormal gait and paralysis in the male breeders since the initiation of the colony. Overall, we have found a variable phenotype in this model, which may be due in part to both the outbred nature of the background strain as well as to possible copy number variation of the transgene.

Onset age can and does differ between individual animals. Onset of abnormal gait and paralysis was observed from approximately 100 – 118 days of age for the first several years; however, as previously reported in 2009 the time of onset of disease was observed to increase, with breeders showing onset of gait problems around 140-165 days and paralysis around 155-170 days. Taconic tracked this change to a genetic bottleneck in the colony wherein the progeny of a very late onset male were used as replacement breeders. Because of this increase in the time of onset of the disease phenotype in the colony at the Taconic facility, we (The ALS Association and Taconic) considered the options for re-starting the line. On consultation with a research group with long experience with this line, we discovered that a similar shift in the age of onset has been experienced in many of the colonies outside Taconic as well. We determined that the age of onset would not be returned to the previously observed range from obtaining stock from external colonies. Subsequently Taconic has rederived the SOD1 colony. The animals used for this derivation were sourced from the existing ALS colony maintained at Taconic. Derivation by embryo transfer and relocation of the SOD1 colony from its original barrier to the new barrier was completed in June 2012. Observations of the current SOD1 colony indicate that onset age still differs among individual animals, and that onset of abnormal gait and paralysis in the male breeders is currently observed from approximately 161-217 days of age.