

**Addendum to the FY2018 APHIS Form 7023 Submission for North Carolina State  
University USDA Registration #55-R-0005 /842**

**Exceptions to Standards Report for the Reporting Period of October 1, 2017 through  
September 30, 2018**

**Species:** Sheep                      **Number affected:** 16

**Exceptions to Standards:** Multiple major survival surgeries- ovariectomy (OVX) was conducted immediately prior to a neurosurgical procedure in 16 sheep. The procedures occurred continuously during the same anesthetic event to prevent re-anesthetizing for two different procedures.

**Standard:** 9CFR Ch.1. Pt.2, Subpt. C. Sec. 2.31 (d) (x) No animal will be used in more than one major operative procedure from which it is allowed to recover, unless: (A) Justified for scientific reasons by the principal, in writing; (B) Required as routine veterinary procedure or to protect the health or well-being of the animal as determined by the attending veterinarian; or (C) In other special circumstances as determined by the Administrator on an individual basis.

**Justification:** In order to investigator minimize variation of endogenous sex steroid levels between animals that alter the neurons that the research targets (GnRH and KNDy neurons), we will OVX female sheep and replace each ewe with a subcutaneous estradiol implant either at the time of surgery or within 1 week prior to experimentation.

**Species:** Sheep                      **Number affected:** 16

**Exception to Standards:** Food restriction- sheep will be food restricted for up to four months to produce a small reduction in body weight (15% of pre-study body weight), These sheep will be initially fed 0.75 x maintenance (calculated at 9.8g/kg/day), but amounts will adjusted weekly to induce an average 15% weight loss over a 50 day period. These sheep will be compared to age matched control animals fed a diet to maintain body weight.

**Standard:** 9CFR Ch.1. Pt.2, Subpt. C. Sec. 2.38 (f) (2) (ii) - Deprivation of food or water shall not be used to train, work, or otherwise handle animals; Provided, however: That the short-term withholding of food or water from animals, when specified in an IACUC-approved activity that includes a description of monitoring procedures, is allowed by these regulations.

**Justification:** This is a procedure that has been used by multiple groups to study the influence of undernutrition on reproduction (Beckett et al., 1997; Hileman et al., 1999; McManus et al., 2005).



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**Species:** Pig                      **Number Affected:** 8

**Exception to Standards:** Multiple major survival surgeries performed. An initial embryo transfer procedure was performed to place transgenic embryos unto the uterus of a recipient, and, approximately 40 days later, a second surgery to access the uterus and inject the developing fetuses with test cells was performed.

**Standard:** 9CFR Ch.1. Pt.2, Subpt. C. Sec. 2.31 (d) (x) No animal will be used in more than one major operative procedure from which it is allowed to recover, unless: (A) Justified for scientific reasons by the principal investigator, in writing; (B) Required as routine veterinary procedure or to protect the health or well-being of the animal as determined by the attending veterinarian; or (C) In other special circumstances as determined by the Administrator on an individual basis.

**Justification:** There is no suitable alternative to this double surgery procedure based on a literature search. The investigators were concerned that non-surgical embryo transfer in swine is highly inefficient with less than 10% success compared to surgically induced rates, resulting in the need for using more swine recipients. Such a low efficiency for success with transgenic embryos, combined with the use of clones, would not allow reliable establishment of pregnancy. There are no known other methods of successful engraftment of cells into developing pig fetuses.

**Species:** Pig                      **Number Affected:** 8

**Exception to Standards:** Large sows recovering from abdominal surgery are housed in a stall measuring 3 x 10 feet. Animals are housed singly until the surgical wound is completely healed (maximum 3-4 weeks), after which time, they are returned to standard housing generally consisting of two sows per 10 x 10 foot pen during the gestation period.

**Standard:** 9CFR Ch.1. Pt.2, Subpt. F. Sec. 3.128 - Enclosures shall be constructed and maintained so as to provide sufficient space to allow each animal to make normal postural and social adjustments with adequate freedom of movement. Inadequate space may be indicated by evidence of malnutrition, poor condition, debility, stress, or abnormal behavior patterns.

**Justification:** The investigators request the exception in order to minimize movement of the animal while the incision is healing and to more closely monitor appetite and recovery. Additionally, this mitigates the concern of fecal contamination of the incision site and post-operative infection.