Summary of Exceptions to the Regulations and Standards

The IACUC has approved protocols that require multiple survival surgeries:

**Procedure for monitoring these activities**

Monitoring plans are developed and approved by the IACUC on a protocol-by-protocol basis. Veterinary technicians observe all animals at a minimum once daily. All husbandry staff monitor animals during the course of their daily activities, and any animals in need of care are brought to the attention of the Attending Veterinarian and/or the veterinary technicians.

**Protocols approved for multiple survival surgeries:**

- a) A protocol is approved to study urinary bladder function following partial bladder outlet obstruction and its reversal in a rabbit model (09-289). Animals undergo partial bladder outlet obstruction (pBOO) and bladders are examined at six different time points. After approximately 2 (early correction) or 4 (late correction) weeks, animals undergo a second surgery to remove the pBOO and a bladder biopsy is performed. The goal of these studies is to determine whether early or late correction of pBOO has an effect upon subsequent bladder function, and to correlate any observed differences with molecular analysis. The importance of having the biopsy at the time of reversal is that it allows for a direct comparison of the tissues from the same animal at two different time points once the obstruction has been reversed and the outcome of the reversal is known. → **Number of rabbits affected for this reporting period:** 0

- b) A protocol is approved to study in utero hematopoietic cell transplantation and prenatal and postnatal engraftment enhancement techniques in a canine model (09-707). At gestational day 37, fetuses undergo in utero bone marrow transplant. In utero bone marrow transplants are performed via ultrasound-guided injections when possible but may require a laparotomy. Bitches deliver puppies naturally, but if necessary, for medical reasons, the IACUC has approved performing C-sections to protect the bitch or the fetuses. Between one and six months of age, some of these puppies undergo skin grafting to assess immune tolerance. The transplantation of bone marrow and hematopoietic stem cells into fetal recipients holds promise for the therapeutic management of many congenital hematologic and immune deficiencies. Transplantation of bone marrow at a prenatal time point takes advantage of the immunologic immaturity of the fetal recipient and theoretically allows for unrelated bone marrow transplantation without the toxic immunosuppression required after postnatal transplantation. → **Number of dogs affected for this reporting period:** 0

- c) A protocol is approved to study in utero hematopoietic cell transplantation and analyze the benefit of differing injection techniques, pre-injection donor cell manipulations, selective myeloablation of the recipient, and postnatal enhancement strategies in a canine model (09-848). At gestational day 33-50, animals undergo a laparotomy for in utero hematopoietic cell transplantation (IUHCT) injections to evaluate differing injection techniques (transuterine ultrasound-guided intraperitoneal, transuterine ultrasound-guided intrahepatic, transuterine ultrasound-guided intravascular, and transuterine ultrasound-guided intracardiac injection). A non-survival repeat laparotomy maybe performed 24 hours, 96 hours or 14 days following the in utero hematopoietic cell transplantation injection for fluorescent cell injection analysis. In case of dystocia, a C-section is approved by the IACUC to protect the bitch or the fetuses. Some of the puppies may undergo skin grafting to assess immune tolerance. → **Number of dogs affected for this reporting period:** 0
d) A protocol is approved to study fetal lung gene therapy techniques in a sheep model (09-878). Animals undergo a laparotomy and hysterotomy to perform temporary fetal tracheal occlusion with surgical suture and administration of viral vector into the lung lumen. Approximately 7-10 days later, a laparotomy and hysterotomy are repeated to remove the fetal tracheal occlusion to ensure fetal survival. The overall goal is to deliver viral vector to fetal ovine lung via direct intra-tracheal injection to determine whether viral vectors have the ability to provide long-term transduction of the fetal lung. The ability to transfer therapeutic genes to the fetal lung has unlimited potential in development of prenatal strategies for lethal lung diseases including cystic fibrosis and surfactant deficiency. → Number of sheep affected for this reporting period: 3
Food or Fluid Restriction
Experimental situations that require food restriction:

<table>
<thead>
<tr>
<th>Title of Experiment</th>
<th>Justification</th>
<th>Species</th>
<th>Length of Restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cardiac Valvuloplasty in Fetal Sheep (08-604)*</td>
<td>Prevention of vomiting and aspiration of stomach contents during anesthetic induction of pregnant sheep.</td>
<td>Sheep</td>
<td>Food withheld for 12-48 hours prior to surgery with unrestricted access to water.</td>
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<tr>
<td>2. Fetal Lung Gene Therapy in Sheep (09-878)</td>
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</tbody>
</table>

* No animals were used for this reporting period.

Number of Sheep Affected for this Reporting Period: 9
(9 were fasted for 24 hours)

Variables that are monitored to ensure animal health during the restricted period.
When sheep are fasted for 12-48 hours, a form is placed on the cage where urine/fecal output is noted daily. If a decrease in fecal or urine output is noted, a Veterinary Technician and/or the Attending Veterinarian is notified.

Steps taken to ensure adequate nutrition/hydration during the restricted period.
The sheep are allowed free access to water at all times. We have not observed detrimental effects in the sheep from food restriction, and have a low rate of complications with survival sheep fetal surgeries.