Summary of Exceptions to the Regulations and Standards

The IACUC has approved protocols that require multiple survival surgeries:

Procedures 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 monitors 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:

1. A protocol is approved to study urinary bladder function following partial bladder outlet obstruction and its reversal in a rabbit model (12-289). Animals undergo partial bladder outlet obstruction (pBOO). 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 (12-289) affected for this reporting period: 22

2. 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 post natal enhancement strategies in a canine model (12-848). At gestational day 38-50, 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). In case of dystocia, a C-section is approved by the IACUC to protect the bitch or the fetuses. Some of the pups may undergo skin grafting to assess immune tolerance. To evaluate tolerance following IUHCT, the protocol is also approved for mother to offspring kidney transplantation.
   
   Number of dogs (12-848) affected for this reporting period: 9

3. Number of rabbits affects this reporting period: 8
4. A protocol is approved to study renal transplantation using a non-human primate model (10-937). The goal of this protocol is to determine the effectiveness of a novel immune suppressive medication that is administered for a short period of time and has the ability to prevent the rejection of the transplanted kidney allograft. Each animal is utilized as a kidney donor then as a recipient. The maximum number of surgeries for any one animal is five: kidney donation; kidney transplantation; possible laparotomy for removal of residual native kidney; and up to 2 possible explorations if renal function deterioration is observed.

Number of non human primates affected for this reporting period: 4

5. A protocol is approved to study in utero repair of Myelomeningocele (MMC) in a sheep model (11-957). The goal of this protocol is to determine whether tissue-engineered constructs can be used to cover MMC defects and prevent progressive destruction of the spinal cord before birth. Between 65-75 days gestation, a surgical procedure is performed to create Myelomeningocele defect (Spina Bifida). Following the creation of Spina Bifida surgically, the spinal cord must be exposed to amniotic fluid for several weeks in order to simulate human Spina Bifida prior to repair. Between 95-105 days gestation, a second surgical procedure is performed to correct the defect. Creation and repair of MMC cannot be accomplished without more than one major survival surgery.

Number of sheep affected for this reporting period: 4

6. A protocol is approved for the study of an immunosuppressive strategy in a non-human primate model of islet transplantation (11-985). The goal of the study is to determine the safety and efficacy of islet transplantation as a treatment for diabetes and diabetes related complications. A major goal of the study is to develop strategies so that patients can accept transplanted islets without the need for long-term immunosuppressive drugs. In this study, the efficacy of novel immune suppressive medicine that is administered for a short period of time is studied. A laparotomy is performed in recipients for islet transplantations. An additional laparotomy is approved to obtain a liver biopsy or pancreas biopsy for evaluation of the morphology of intrahepatic islet allografts or the native islets within the pancreas, respectively. The surgeries are necessary to evaluate the function of the transplantation. An additional laparotomy is approved for a second islet transplantation to allow for further investigation into the use of islet transplantation as a better treatment for humans with diabetes mellitus.

Number of NHP affected for this reporting period: 0
### 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>
<th>Number of animals affected this reporting period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Lung Gene Therapy in Sheep (12-878)</td>
<td>Prevention of vomiting and aspiration of rumen 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>
<td>5</td>
</tr>
<tr>
<td>In Utero Repair of Myelomeningocele in Sheep (11-957)</td>
<td>Prevention of vomiting and aspiration of rumen 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>
<td>4</td>
</tr>
<tr>
<td>Bone Transport - Repairing Large Cranial Defects with a Novel Bone Transportation System (11-961)</td>
<td>Prevention of vomiting and aspiration of rumen 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>
<td>12</td>
</tr>
<tr>
<td>Fetal Lung Sclerotherapy in Sheep (12-995)</td>
<td>Prevention of vomiting and aspiration of rumen 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>
<td>2</td>
</tr>
</tbody>
</table>

Animals are monitored twice daily during restricted period to ensure adequate nutrition and hydration. When sheep are fasted for 12-48 hours, a form is placed on the cage and urine/fecal output is noted daily. If a decrease in fecal or urine output is noted, a veterinary technician or veterinarian is notified.

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.