# ANNUAL REPORT OF RESEARCH FACILITY

## TYPE OR PRINT

### 3. REPORTING FACILITY

(List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

See Attached Listing

<table>
<thead>
<tr>
<th>FACILITY LOCATIONS/site(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(b)(2)High, (b)(7)f</td>
</tr>
</tbody>
</table>

### REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY

(Attach additional sheets if necessary or use APHIS FORM 7023A)

<table>
<thead>
<tr>
<th>A. Animals Covered By The Animal Welfare Regulations</th>
<th>B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.</th>
<th>C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or pain-relieving drugs.</th>
<th>D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving pain or distress to the animals and for which appropriate pain-relieving drugs or tranquilizing drugs were used.</th>
<th>E. Number of animals upon which teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report.)</th>
<th>F. TOTAL NO. OF ANIMALS (Cols. C + D + E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Dogs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>613</td>
</tr>
<tr>
<td>5. Cats</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>6. Guinea Pigs</td>
<td></td>
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<tr>
<td>7. Hamsters</td>
<td>124</td>
<td>153</td>
<td>261</td>
<td>199</td>
<td>613</td>
</tr>
<tr>
<td>8. Rabbits</td>
<td></td>
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<td>9. Non-Human Primates</td>
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<tr>
<td>10. Sheep</td>
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<td>11. Pigs</td>
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<tr>
<td>12. Other Farm Animals</td>
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<tr>
<td>13. Other Animals</td>
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</tbody>
</table>

### ASSURANCE STATEMENTS

1. Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2. Each principal investigator has considered alternatives to painful procedures.

3. This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all the exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4. The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

### CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above is true, correct, and complete in every respect.

(b)(6), (b)(7)c

DATE SIGNED: 6/16/06

[Signature]

[Printed Name]

[Title]
Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 23-R-0064

2. Number ___________________ of animals used in this study.

3. Species (common name) Syrian Hamster of animals used in the study.

4. Explain the procedure producing pain and/or distress.
   Hamsters were food deprived between 6–48 hours without anesthetics or analgesia.
   Please see attached "Exemption from Feeding Standard."

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

   Agency ___________________ CFR ___________________
* EXEMPTION FROM FEEDING STANDARD 11/17/06*

In some experiments, animals are exempt from the feeding standard and analgesics are not administered. The exemption from feeding standard was approved because a body of research supported the contention that the 48 hours of food deprivation or food restriction in sheep did not cause pain and distress, and the animals maintained healthy equilibrium at a lower body fat content. Caloric restriction is used in our laboratory because we are studying the mechanisms that animals use to save energy during periods of low food availability to save energy by inhibition of the reproductive system. Nutritional infertility is an adaptive process whereby animals increase the ability to survive by redistributing their energy economy. Metabolic fuels are shunted away from reproductive processes such as steroid production and mating, and are used for survival (Merry and Holehan, 1979; Merson and Kirkpatrick, 1981, Bronson, 1989). Animals have a sensory system designed to detect internal energy availability (Schneider, 1992). The sensory detectors of fuel availability send signals to parts of the brain that control fertility and ovulation as well as those areas that control hunger, food intake and caloric homeostasis. My experiments are designed to study the mechanisms that underlie this link between energy and fertility. The exemption from feeding standard allows hamsters and sheep to be fasted or food restricted to a degree that induces infertility and anestrus, but not to a degree that causes health problems.*

A 48-hour period of food deprivation has been commonly employed in research on rodents such as hamsters for many years (e.g., Roland et al., 1982; Schneider and Wade, 1989; Morin, 1986). For example, Dr. Morin (Morin, 1986) found that a 48-hour fast on days 1 and 2 of the estrous cycle induced anestrus, but this fast had no other health effects. Hamsters have a 4-day estrous cycle with ovulation and estrous behavior occurring on Day 4. One important piece of evidence demonstrating that a 48 h of fast is not harmful to Syrian hamsters is that when the 48 hour fast occurs on Days 2 and 3, Days 3 and 4, or on Days 4 and 1 or the cycle, there is no effect on estrous cyclicity (the hamsters showed normal ovulation rates and vigorous sex behavior). Ovulation and estrous behavior are inhibited only when the fast occurs on Days 1 and 2 of the estrous cycle, but not on any other days. Morin also found that normal estrous behavior could be easily reinstated in the 48 hour-fasted hamsters by giving an injection of estradiol.

Furthermore, the effects on estrous cyclicity are rapidly reversed when the hamsters are returned to ad lib feeding. I subsequently demonstrated that the same 48-hour fast had no effect on estrous cyclicity or health in previously fattened hamsters (Schneider and Wade, 1989). Thus, a 48 hour fast has no effect on estrous cyclicity whatsoever when the hamsters have a high body fat content. In general, the fatter the hamster, the longer the period of food restriction necessary to induce anestrus. In sheep, much of the information comes from the work of my collaborator on adult ewes, (e.g., Henry et al., 2001, 2004), or for peripubertal sheep from the laboratory of [redacted]. Technically, it does not violate the feeding standard because sheep eat one meal per day, and thus, this procedure does not require an exemption.

Analgesics are not appropriate because we are measuring indices of estrous cyclicity, which is under control of hypothalamic luteinizing hormone releasing hormone (LHRH), also known as gonadotropin releasing hormone (GnRH). LHRH and LH levels are adversely affected by opiates because it is well-known that opiates and opiate
derivatives, including analgesics such as buprenorphine, butorphenol and morphine, affect pituitary hormone secretion and hypothalamic LHRH (References 6-17 below). It is unreasonable to think that aspirin or nonsteroidal anti-inflammatory agents would be effective as analgesics on food deprived hamsters.

References