This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 35-R-0001 **CUSTOMER NO.** 616

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

UNIVERSITY OF WISCONSIN-MADISON
DIRECTOR RESEARCH ANIMAL RESOURCES CENTER
1710 UNIVERSITY AVENUE 396 ENZYME INST
MADISON, WI 53726-4087

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.)

FACILITY LOCATIONS*(sites)*

(b)(2)High, (b)(7)f

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	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.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	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)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	15	155	518		673
5. Cats	3	80	58		138
6. Guinea Pigs		2			2
7. Hamsters		863	199		1062
8. Rabbits	7	21	108		129
9. Non-Human Primates	670	1363	627		1990
10. Sheep	31	11	90		101
11. Pigs	104	74	376		450
12. Other Farm Animals					
cows	125	16	44		60
13. Other Animals					
wild-caught mice	1155	1543	105		1648
skunks		12			12
opossums			5		5

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 (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		11/21/2005

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NO. 35-R-0001 **CUSTOMER NO.** 616

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

UNIVERSITY OF WISCONSIN-MADISON
DIRECTOR RESEARCH ANIMAL RESOURCES CENTER
1710 UNIVERSITY AVENUE 396 ENZYME INST
MADISON, WI 53726-4087

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use this form.)*

A. Animals Covered By The Animal Welfare Regulations	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.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	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)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
horses	12		15		15
raccoons	12	12	12		24
deer			14		14
gerbils		40	48		88
chinchillas		18	56		74
ferrets		9	119		128
squirrels	111	15	139		154

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 (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		11/21/2005

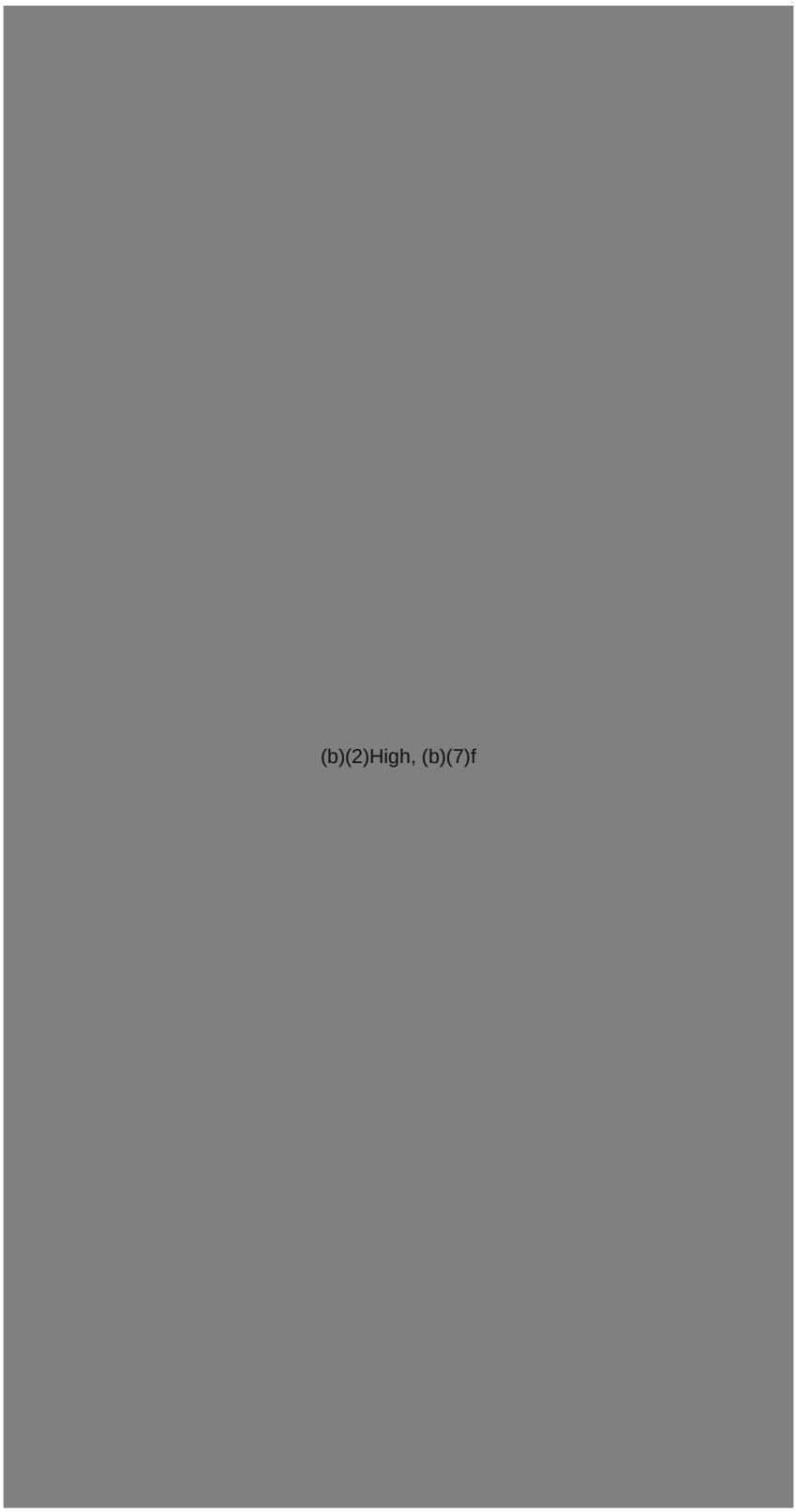
APHIS FORM 7023A (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete

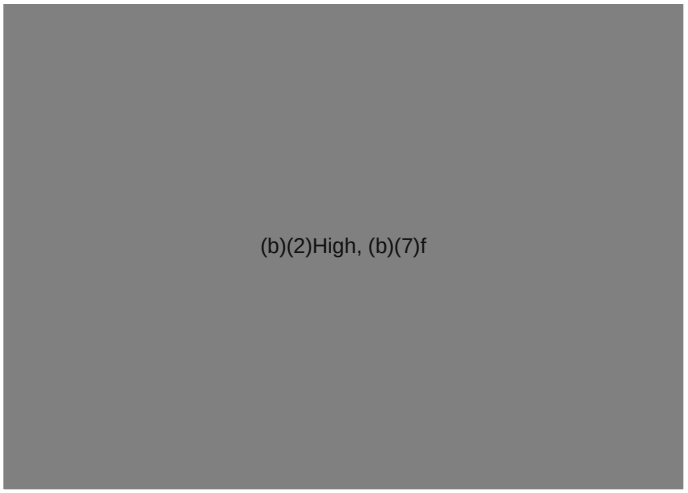
PART 1 - HEADQUARTERS

APHIS Form 7023 Additional Reported Sites

The following additional sites have been reported by the facility. The reported sites have not been verified by APHIS and have been provided by the facility solely for completeness of the APHIS Form 7023 Annual Reporting submission.

Registration Number: 35-R-0001
Customer Number: 616
Facility: UNIVERSITY OF WISCONSIN-MADISON
DIRECTOR RESEARCH ANIMAL RESOURCES CENTER
1710 UNIVERSITY AVENUE 396 ENZYME INST
MADISON, WI 53726-4087




(b)(2)High, (b)(7)f

Annual Report not received yet.

35-R-0001
#616.

NOV 3 2005

SUMMARY OF IACUC APPROVED EXCEPTIONS TO THE STANDARDS AND REGULATIONS OF THE USDA ANIMAL WELFARE ACT

University of Wisconsin-Madison
Registration No.: 35-R-0001
Reporting Period: 10/01/04 – 09/30/05

More Than One Protocol Involving a Major Operative Procedure:

While there are some protocols containing multiple surgical procedures, there are no approved protocols for use of animals across protocols and involving major operative procedures.

Food and/or Water Deprivation:

- IACUC approved protocol for up to 156 Rhesus and 100 Hamsters – water restriction for up to 12 hours/day for five days for Conditioned Taste Aversion Training.
- IACUC approved protocol for up to 154 Rhesus – 30% dietary restriction over years to determine effects on aging.
- IACUC approved protocol for up to 145 marmosets – 15-18 hour overnight food restriction to provide physiological stressor to adrenal cortisol.
- IACUC approved protocol for up to 70 cats and 8 Rhesus – water restriction as part of work reward for up to 18 hours per day for 6 days.
- IACUC approved protocol for up to 24 Rhesus – 12 hour fast prior to vitamin A dosing and metabolic cage housing.
- IACUC approved protocol for up to 35 Rhesus – limited to food 2 times per day with a maximum fasting period of up to 20 hours for calorimetric studies.
- IACUC approved protocol for up to 350 Rhesus – 24 hrs. or less food restriction once per week for up to four weeks is not performing during learning test paradigm for five days in a row.
- IACUC approved protocol for up to 20 rhesus and 20 marmosets – animals fasted from 4pm to 8am for analysis of luminal contents.
- IACUC approved protocol for up to 47 Rhesus – animals fasted from 4pm to 8 or 10 am to prevent stool accumulation in rectum for SIV low dose challenge i.r.
- IACUC approved protocol for up to 15 Rhesus – 14-16 hour overnight fast for accurate caloric intake measurement.
- IACUC approved protocol for up to 8 Rhesus – 2-9 days of receiving only one meal that is of the amount typically eaten *ad libidum* in 1.5 hours.
- IACUC approved protocol for up to 54 Rhesus – overnight fast up to 20 hrs. to prevent accumulation of stool in rectum before SIV challenge i.r.
- IACUC approved protocol for up to 15 Rhesus – maximum 16 hr. overnight fast to increase motivation prior to behavioral testing.
- IACUC approved protocol for up to 10 Rhesus – animals receive weighed amount of chow for 8 hrs/day followed by overnight fasting for calorimetric studies.
- IACUC approved protocol for up to 120 Sheep – food totally withheld during 2 hrs for-3 days exposure to hyperbaric pressure chamber to prevent excessive gas production.
- IACUC approved protocol for up to 9 Rhesus – overnight food fast for effective tracer in PET scans.

- IACUC approved protocol for up to 60 Dogs – periodic overnight food fast to determine blood glucose levels.
- IACUC approved protocol for up to 150 Ground Squirrels – maximum of 9 hrs. fluid restriction due to holding in traps before release for testing.
- IACUC approved protocol for up to 60 Hamsters – animals fasted for 4 hrs. prior to bleeding for in vivo experiments.
- IACUC approved protocols for up to 27 Rhesus – daily water and juice intake controlled and then used as a motivator for learning.
- IACUC approved protocols for up to 125 Rhesus - Fasted for up to 20 hours prior to blood collections.
- IACUC approved protocols for up to 10 Rhesus - No access to food during up to 8 hrs. of chairing. Treats are given periodically during chairing.
- IACUC approved protocols for up to 8 Rhesus - Up to 16hr. overnight food and water restriction as motivator prior to training/testing sessions (only done if necessary).
- IACUC approved protocols for up to 3 Rhesus - Receive weighed amount of chow (more than they are expected to eat) for 8 hrs/day followed by overnight fasting for calorimetric studies (for up to 39 weeks).
- IACUC approved protocols for up to 20 Rhesus - Max. 16 hr. overnight food fast to increase motivation prior to behavioral testing.
- IACUC approved protocols for up to 4 Rhesus - Fasted for up to 18 hours prior to all blood draws (2-3 per week for up to three months).
- IACUC approved protocols for up to 30 Cynomolgus - Max. 16 hr. overnight food fast to increase motivation prior to behavioral testing.

Not Cleaning and/or Sanitizing at Required Frequencies:

- IACUC approved protocol for up to 276 13-lined ground squirrels – exempted from cage cleaning during hibernation period.
- IACUC approved protocol for up to 60 Rhesus – limited cage cleaning for up to three weeks after receiving radioactive materials (clean pans only).
- IACUC approved protocol for up to 130 Tamarins – cages cleaned every 2-3 months in order to allow for natural marking behavior.
- IACUC approved protocol for up to 15 Rhesus - Animals will be isolated for 72 hours without cage cleaning following MPTP administration.
- IACUC approved protocol for up to 5 Rhesus - Animals will be isolated for 72 hours without cage cleaning following MPTP administration.
- IACUC approved protocol for up to 20 Rhesus - Animals will be isolated for 72 hours without cage cleaning following MPTP administration.
- IACUC approved protocol for up to 30 Cynomolgus - Animals will be isolated for 72 hours without cage cleaning following MPTP administration.

Restraint:

- IACUC approved protocol for up to 136 sheep – tethering of post-surgical animals in portable enclosures for up to 10 days to prevent damage to surgical instrumentation.
- IACUC approved protocol for up to 125 Rhesus – jacket and tether restraint of animals for up to 72 hours for serial blood sampling of unstressed, unanesthetized monkeys.

- IACUC approved protocol for up to 350 Rhesus – chair restraint for up to 3 hours to measure and map sleeping brain activity.
- IACUC approved protocol for up to 288 Sheep – ovariectomized sheep placed in 56"Lx25"Wx25"H carts for up to 10 days to prevent chewing catheters.
- IACUC approved protocol for up to 47 Cynomolgus Macaque – chair restraint with pole and collar to perform multiple procedures.
- IACUC approved protocol for up to 10 Rhesus - chairing up to 8 hrs. with minimum of 35 hrs between chairings. Chairing is necessary to allow placement of surface thermistors and ECG electrodes.
- IACUC approved protocol for up to 8 Rhesus - chairing and head restraint for up to 3 hrs. for microelectrode measurements.
- IACUC approved protocol for up to 16 Marmosets - animals will be confined to a small chamber (15 cm x 20 cm x 15 cm) for up to one hour as a mild experimental stressor. Animals will be Velcro strapped to a padded board for up to one hour as a moderate experimental stressor.
- IACUC approved protocol for up to 36 Marmosets - animals will be restrained in a special restraint device that prohibits any movement of the head and body for up to 3 hours during fMRI scans.
- IACUC approved protocol for up to 30 Rhesus - animals are chaired for up to 1.5 hours as an experimental stressor.

Housing:

- IACUC approved protocol for up to 15 Rhesus – eight week single housing for surgical healing (5 weeks) and experimental adaptation (3 weeks).
- IACUC approved protocol for up to 47 Cynomolgus Macaque – housed individually for 1 week following surgery until skin incision is fully healed.
- IACUC approved protocol for up to 145 Rhesus - Housed singly for up to 7 hours per day for food intake measurements. Also housed singly for up to 72 hours once per month for urine collection and serial blood sampling.
- IACUC approved protocol for up to 154 Rhesus - Housed singly for their lifetime to ensure accurate measurement of food intake.
- IACUC approved protocol for up to 10 Rhesus - Housed singly for up to 4 months to enable urine collection; exposed to cooler (66.2F) and warmer (91.4 F) temperatures for up to 8 hours, 2-3 times per week
- IACUC approved protocol for up to 67 Rhesus and 30 cynomolgus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 30 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 30 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination

between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.

- IACUC approved protocol for up to 45 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 20 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 74 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 36 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 20 Rhesus and 20 Marmosets - Housed singly for up to 30 hours to collect urine.
- IACUC approved protocol for up to 30 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 30 Cynomolgus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 16 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 15 Rhesus - Housed singly for the duration of the experiment (up to 34 weeks) to ensure accurate measurement of food intake.
- IACUC approved protocol for up to 20 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination

between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.

- IACUC approved protocol for up to 48 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 8 Rhesus - Housed singly for duration of the experiment for daily water regulation.
- IACUC approved protocol for up to 40 Cynomolgus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 30 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 30 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 54 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 15 Rhesus - Housed singly for the duration of the experiment to assure conformity with the earlier portion of this study done at another institution.
- IACUC approved protocol for up to 53 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 40 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 14 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination

between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.

- IACUC approved protocol for up to 5 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 84 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 5 Rhesus - Housed singly for 72 hours following MPTP administration. 10 Rhesus - Housed singly for the duration of the experiment (up to 12 weeks) to ensure accurate measurement of food intake.
- IACUC approved protocol for up to 35 Rhesus - Housed singly for the duration of the experiment (up to 20 weeks) to ensure accurate measurement of food intake.
- IACUC approved protocol for up to 3 Rhesus - Housed singly for the duration of the experiment (up to 39 weeks) to ensure accurate measurement of food intake.
- IACUC approved protocol for up to 20 Rhesus - Housed singly for 72 hours following MPTP administration and for 24 hours following FDOPA PET scans.
- IACUC approved protocol for up to 50 Rhesus - Housed singly for their lifetime after SIV infection to prevent the following: 1) to prevent the spread of cross contamination between animals infected with different viral strains, 2) to prevent cross contamination between animals who are at different stages of SIV infection, and 3) to prevent spread of opportunistic infections commonly associated with SIV infection.
- IACUC approved protocol for up to 4 Rhesus - Housed singly for up to 3 months to enable urine collection.
- IACUC approved protocol for up to 30 Cynomolgus - Housed singly for 72 hours following MPTP administration, for 15 days following steriotaxic injections, and for 24 hours following FDOPA PET scans.
- IACUC approved protocol for up to 5 Marmosets - Housed singly while on treatment for neurologic dysfunction (up to several weeks).