This report is required by law (7 USC 2143). Failure to comply according to the regulations

See reverse side of this form for additional information

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 14-R-0027
CUSTOMER NUMBER: 123

FORM APPROVED
OMB NO. 0579-0036

# ANNUAL REPORT OF RESEARCH FACILITY

( TYPE OR PRINT )

Avant Immunotherapeutics, Inc.
119 Fourth Avenue
Needham, MA 02194

Telephone: (617) -433-0771

NOV 26 2002

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

**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 ye | 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, a | 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 | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | 145 | | 37 | 182 |
| 7. Hamsters | | | | | |
| 8. Rabbits | | 70 | 22 | | 92 |
| 9. Non-human Primate | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, 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 such 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

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
( Chief Executive Officer or Legally Responsible Institutional Official )

Print

DATE SIGNED 11/20/02

( AUG 91 )

EG 12/2/02

Special Use:

## 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: 14-R-0027

2. Number 37 of animals used in this study.

3. Species (common name) GUINEA PIG of animals used in the study.

4. Explain the procedure producing pain and/or distress.

DEATH MAY RESULT DURING THE PERFORMANCE OF A GENERAL SAFETY TEST PER 21 CFR 610.11.

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)

FOLLOWING FEDERALLY MANDATED TESTING. SEE 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 FDA CFR 21 CFR 610.11

AND FDA GUIDANCE MEMORANDUM "PROPOSAL TO DEVELOP GUIDELINES TO ESTABLISH UNIFORMITY IN GENERAL SAFETY TEST" OF 2/3/94

This report is required by law (7 USC 2143). Failure to report ing to the regulations can result in an order to cease and desist and to be subject to penal as provided for in Section 21! NOV 16 2004 See d form for additi nformation. Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 14-R-0027
CUSTOMER NUMBER: 123

FORM APPROVED
OMB NO. 0579-0036

Avant Immunotherapeutics, Inc.
119 Fourth Avenue
Needham, MA 02194

Telephone: (617) -433-0771

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

119 FOURTH AVE., NEEDHAM, MA 02494 FACILITY LOCATIONS ( Sites ) - See Atached Listing

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

| A. Animals Covered By The Animal Welfare Regulations | B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | 36 | | 8 | 44 |
| 7. Hamsters | | | | | |
| 8. Rabbits | | 101 | 90 | | 191 |
| 9. Non-human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc 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 )

SIGNAT

or Print ) DATE SIGNED 11/9/04

APHIS FC
( AU(

## 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: 14-R-0027

2. Number 8 of animals used in this study.

3. Species (common name) GUINEA PIG of animals used in the study.

4. Explain the procedure producing pain and/or distress.

DEATH MAY RESULT DURING PERFORMANCE OF A GENERAL SAFETY TEST PER 21 CFR 610.11

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)

FOLLOWING FEDERALLY MANDATED TESTING (SEE 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 FDA CFR 21 CFR 610.11

AND FDA GUIDANCE MEMORANDUM "PROPOSAL TO DEVELOP GUIDELINES TO ESTABLISH UNIFORMITY IN GENERAL SAFETY TEST" OF 2/3/94

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 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.** 14-R-0126 **CUSTOMER NO.** 155

FORM APPROVED
OMB NO. 0579-0036

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

ADVANCED MAGNETICS INC.
61 MOONEY STREET
CAMBRIDGE, MA 02138
(617) 497-2070

**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)*

See Attached Listing

**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 | — | — | — | — | — |
| 5. Cats | — | — | — | — | — |
| 6. Guinea Pigs | — | — | — | — | — |
| 7. Hamsters | — | — | — | — | — |
| 8. Rabbits | — | — | 11 | — | 11 |
| 9. Non-Human Primates | — | — | — | — | — |
| 10. Sheep | — | — | — | — | — |
| 11. Pigs | — | — | — | — | — |
| 12. Other Farm Animals | — | — | — | — | — |
| | | | | | |
| 13. Other Animals | — | — | — | — | — |
| Rats | — | — | 77 | 140 | 217 |
| | | | | | |
| | | | | | |

**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)

SI

DATE SIGNED 10/15/01

AF

1 - HEADQUARTERS

(AUG 91)

# Column E Explanation

**Registration Number: 14-R-0126**

**Explanation and scientific justification:**

Background

The company conducts research in animals as part of the development process for new drug products used in the diagnosis of cancer and other diseases. The new drug products developed at Advanced Magnetics are "new chemical entities", that is they are new molecular materials and there is no existing knowledge of their toxicologic or pharmacologic properties.

Procedure:

All animals listed in Column E were used to evaluate the propensity of test materials to (b)(4) (b)(4) following a single intravenous administration. Rats are administered a single tail vein injection of the test material. The (b)(4) (b)(4) The rat is known to respond to intravenous administration of pharmaceuticals that are chemically similar in composition to the drugs that are being tested. The formation of (b)(4) (b)(4) (b)(4) This evaluation is used in determining the relative safety of pharmaceutical products under development. The drug products tested *may* cause (b)(4) and this subsequently may cause discomfort to the animal, however, the end-point measurement is the actual (b)(4) as measured by an instrument called a (b)(4) Therefore, pharmacologic/therapeutic intervention to inhibit (b)(4) would interfere with the conduct of the study and the actual endpoint determination. No alternative to this is possible.

Regulatory Considerations:

For new chemical entities and other drugs whose clinical safety and efficacy have not been established, preclinical or nonclinical in vitro and in vivo animal testing is required by the U.S. Food and Drug Administration (FDA) prior to clinical study in humans and ultimately FDA approval for marketing. In recent years there has been an international effort between the FDA, the European Union and Japan to "harmonize" the worldwide regulatory requirements for new drug development. This effort has resulted in the International Conference for Harmonization (ICH) which also issues guidelines for nonclinical drug testing.

FDA requirements are contained in Title 21 of the CFR. In the drug development process drugs are first investigated in human clinical studies after the submission of an Investigational New Drug Application (IND) to the FDA. FDA regulations in 21 CFR Part 312 require that adequate information about pharmacological and toxicological studies of the drug involving laboratory animals that show that it is reasonably safe to conduct clinical investigations must be provided. As drug development proceeds, additional information pertinent to the safety of the drug must be provided depending on the nature of the drug and the clinical investigations. A description of the toxicological effects of the drug in animals must be provided and must include the results of acute, subacute, and chronic toxicity tests; tests of the drug's effects on reproduction and the developing fetus; any special toxicity test related to the drug's particular mode of administration or conditions of use; and any in vitro studies to evaluate drug toxicity.

This report is required by law (7 USC 2143). Failure ort according to the regulations can result in an order to cease and desist and to be subj , penalties as provided for in Section 2150. See revers for additional i ation. 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.** 14-R-0126 **CUSTOMER NO.** 155

FORM APPROVED
OMB NO. 0579-0036

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

ADVANCED MAGNETICS INC.
61 MOONEY STREET
CAMBRIDGE, MA 02138

**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)*

ADVANCED MAGNETICS INC.
CAMBRIDGE, MA 02138

**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 | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | | | | |
| 7. Hamsters | | | | | |
| 8. Rabbits | | | 11 | | 11 |
| 9. Non-Human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
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**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 |
|---|---|---|
| | | 11/07/2001 |

**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 repo rding to the regulations See attar rm for additiona. nation Interagency Report Control No.:
can

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 21-R-0114
CUSTOMER NUMBER: 336

FORM APPROVED
OMB NO. 0579-0036

Weill Medical College Of Cornell University
1300 York Avenue
Box 40
New York New York, NY 10021

DEC 02 2002

Telephone: (212) -746-1022

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 ye | 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, a | 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 | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | --- | 25 | ---- | 25 |
| 5. Cats | | --- | 14 | ---- | 14 |
| 6. Guinea Pigs | | 149 | 39 | ---- | 188 |
| 7. Hamsters | | --- | 116 | ---- | 116 |
| 8. Rabbits | | 18 | 78 | 87 | 183 |
| 9. Non-human Primate | | --- | 11 | 6 | 17 |
| 10. Sheep | | --- | 2 | ---- | 2 |
| 11. Pigs | | --- | 142 | ---- | 142 |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, 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 such 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

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
( Chief Executive Officer or Legally Responsible Institutional Official )

| NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *( Type or Print* | DATE SIGNED |
|---|---|
| | 11/25/02 |

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

KJCC

**APHIS Form 7023 Site List**

The following sites have been reported by the facility.

Registration Number: 21-R-0114
Customer Number: 336
Facility: WEILL MEDICAL COLLEGE
1300 YORK AVENUE
NEW YORK NEW YORK, NY 10021
(212) 746-1077

BURKE MEDICAL RESEARH INSTITUTE
785 MAMMARONECK AVE
WHITE PLAINS, NY 10605

HARKNESS BLDG
HARKNESS AND S BLDG. AND C BUILDING
1300 YORK AVE
NEW YORK NEW YORK, NY 10021

KIPS BAY BUILDING
411 E. 69th ST., BASEMENT
NEW YORK, NY 10021

BOURNE LABORATORY
21 BLOOMINGDALE ROAD
WHITE PLAINS, NY 10605

KETTERING LABORATORY BUILDING
425 E. 68th ST., 3rd Floor
NEW YORK, NY 10021

Weill Medical College of Cornell University
"Reportable IACUC-Approved Exceptions"

Deprivation of water in non-human primates (for behavioral training) = 2 protocols

USDA Report WMC/CU
Certificate # 21-R-0114
11/25/02

## Optional Column E Explanation Form

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: 21-R-0114

2. Number 6 of animals used in this study.

3. Species (common name) Non-Human Primate of animals used in this study.

4. Explain the procedure producing pain and/or distress.

   The animals will be placed on a water restriction regime during the on-control periods of research. Although a detailed method of evaluation has been successfully employed since the inception of the protocol, it is possible that the animals could become dehydrated during the on-control periods. If the animal becomes dehydrated, the animal will be treated appropriately with rehydrating fluids. In addition, visual behavior experiments require that the monkey be restrained for several hours a day in a primate chair. The restraint could be distressful. Precautions are taken to prevent the animal from experiencing pain or distress while in the primate chair. Excessive grimacing, vocalizations or squirming may be signs that the animal is uncomfortable in the chair. If these behaviors are displayed during a recording session, the experiment for that day will be terminated and the animal returned to its cage.

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 question 6 below).

   Pain or distress will be relieved by rehydrating the monkey in the case of dehydration and removal from the primate chair if the animal displays signs of discomfort or pain. Although appropriate action would be taken immediately, the animals were placed in category E because both of these situations may occur.

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_____

## Optional Column E Explanation Form

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: 21-R-0114

2. Number 87 of animals used in this study.

3. Species (common name) Rabbits of animals used in this study.

4. Explain the procedure producing pain and/or distress.

   The (b)(4) of these animals is unilaterally excised to induce (b)(4) in the hind leg. Ten days after the surgery the animal is injected with a viral vector that expresses vascular (b)(4) growth factor to induce (b)(4). Ten days after the injection a angiogram is performed and the animal is sacrificed. The investigators are looking at a potential alternative to coronary bypass or angioplasty.

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 question 6 below).

   The (b)(4) in the hind leg may induce (b)(4) despite the collateral circulation that is present. This condition can cause distress and could ultimately lead to automutilation of the foot. The animals are placed on (b)(4) for 5 days post-operatively. In case of autotomy the treatment would be continued as long as needed. However, it is unclear if (b)(4) (or any other analgesic) is able to relieve the paresthesia. The animals were therefore placed into category E preemptively.

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_____

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 21!

DEC 0 2 2003

See attached form for additional information.

Interagency Report Control No.

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 33-R-0029
CUSTOMER NUMBER: 603

FORM APPROVED
OMB NO. 0579-0036

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

University Of Illinois At Urbana-Champaign
1 Observatory Building
901 S. Mathews
Urbana, IL 61801

Telephone:

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz 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 a the reasons such drugs were not used must be attached this report ). | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | 24 | 102 | 29 | | 131 |
| 5. Cats | 7 | 4 | 1 | | 5 |
| 6. Guinea Pigs | 16 | 28 | 4 | 12 | 44 |
| 7. Hamsters | 2 | 12 | 44 | | 56 |
| 8. Rabbits | 60 | 24 | 261 | | 285 |
| 9. Non-human Primates | | 3 | | | 3 |
| 10. Sheep | | | | | |
| 11. Pigs | 55 | | 24 | 130 | 154 |
| 12. Other Farm Animals | | | | | |
| Bovine | 42 | 39 | 14 | | 53 |
| 13. Other Animals | | | | | |
| Equine | 23 | 23 | 28 | | 51 |
| Chinchilla | 9 | | 8 | | 8 |
| Gerbil | 77 | | 78 | | 78 |

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary inc 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
ief Executive Officer or Legally Responsible Institutional Official )

| SIGNATU | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL ( Type or Print ) | DATE SIGNED |
|---|---|---|
| | | 11/26/03 |

APHIS FO ...hich is obsolete.)
( AUG 91 )

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. Approved Agency Report Control No. 0180-0OA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO.

FORM APPROVED
OMB NO. 0579-0036

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

# CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

*( TYPE OR PRINT)*

**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 — 12. &/OR 13. Other *(List by species)* | 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) |
|---|---|---|---|---|---|
| Bat | 5 | | 37 | | 37 |
| Ferret | | | 49 | | 49 |
| Caprine | | 3 | | | 3 |
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**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 such 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 | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)* | DATE SIGNED |
|---|---|---|
| | | 11/26/03 |

APHIS

## 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: **33-R-0029**

2. Number 12 of animals used in this study.

3. Species (common name) Guinea pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

**The animals were given free access to food. Half the animals were given salt (500 mM final) in their drinking water while the control animals received tap water. This causes a bit of "stress" to the animals. The ones given salt water drink less, eat less and lost some weight.**

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 question 6 below)

**The protocol employed was adapted from others in the literature. It is designed to cause osmotic imbalance in the kidney triggering mechanisms to retain water and release sodium.**

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_____

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: **33-R-0029**

2. Number 42 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

Colostrum deprived piglets (n=42) were infected with rotavirus on day 2 postpartum which resulted in a self-limiting diarrhea of 8-10 day duration. Animals experienced a voluntary reduction in food intake and a transient weight loss, which was recovered within 4-6 days postinfection. Signs of dehydration were treated by administration of oral rehydration solution.

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 question 6 below)

Although animals experienced pain and/or distress due to RV infection, we believe that it is not severe. The goal of our study is to determine how (b)(4) (b)(4) Administration of pain-relieving drugs (b)(4) (b)(4) which would preclude our ability to determine the impact of (b)(4)

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

## Column E Explanation

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1. Registration Number: **33-R-0029**

2. Number 40 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

**Pigs were infected with PRRSV.**

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 question 6 below)

**The purpose of the study was to investigate strategies to inhibit the morbidity effects of PRRSV infection. Currently, there is no approved treatment for PRRSV infection.**

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_____

**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: **33-R-0029**

2. Number **40** of animals used in this study.

3. Species (common name) **Pigs** of animals used in the study.

4. Explain the procedure producing pain and/or distress.

**Pigs were infected with PRRSV.**

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 question 6 below)

**The purpose of the study was to investigate strategies to inhibit the morbidity effects of PRRSV infection. Currently, there is no approved treatment for PRRSV infection.**

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_____

## 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: **33-R-0029**

2. Number **8** of animals used in this study.

3. Species (common name) **Pigs** of animals used in the study.

4. Explain the procedure producing pain and/or distress.

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 question 6 below)

**The pigs are listed in a Pain/No Drug category; however, transient mild discomfort in some animals would be a more appropriate term. The animals are not given drugs as the administration of analgesic would cause as much or more discomfort as the administration of the experimental inoculum.**

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_____

Customer ID and Site Address: University of Illinois
1 Observatory
901 S. Mathews
Urbana, IL 61801
(phone)
(fax)

ID: 603

Facilities reported

Beckman Institute of Advanced Science and Technology
Burrill Hall
Morrill Hall
Medical Sciences Building
Psychology
Edward R. Madigan Laboratory
Veterinary Medicine Basic Sciences Building
Veterinary Medicine Small Animal Clinic
Veterinary Medicine Large Animal Clinic
Veterinary Medicine Research Farm

UNIVERSITY OF ILLINOIS
AT URBANA-CHAMPAIGN

Division of Animal Resources

1 Observatory Building
901 South Mathews Avenue
Urbana, IL 61801

July 15, 2004

Robert A. Willems, DVM
Regional Animal Care Specialist
Eastern Region, Animal Care, USDA
920 Main Campus Drive
Suite 200
Raleigh, NC 27606

RE: Annual Report Addendum

Dear Dr. Willems:

As per your request, I am including further information concerning 3 sets of animals listed in Column E of our 2003 Annual Report.

1. Twelve guinea pigs were provided a NaCl solution as their sole source of drinking water for 3 days to induce dehydration/increased tonicity. Guinea pigs are similar to humans in that they express the enzyme, BHMT, in the kidney. They were used in an experiment to study the effects of this enzyme, which is thought to play a role in protecting kidney cells if an animal becomes dehydrated. The IACUC was concerned about the potential to induce distress if significant dehydration developed. Body weights were measured daily and the animals were monitored at least every 8 hours to ensure intervention would occur if established endpoints were reached. It was noted during the course of the experiment that the animals did eat less and drank less than controls, but only lost approximately 10% of their body weight (endpoint - 20%). The guinea pigs developed only mild-to-moderate dehydration, which was sufficient for the experiment and any distress was considered to be minimal.

2. Two groups of 40 pigs, used in experiments to study in a controlled setting how common infectious disease affects growth and performance in swine, were infected with PRRSV (porcine reproductive and respiratory syndrome virus). As intended, this infection did induce a clinical disease in the pigs comparable to a mild respiratory flu in humans. The pigs continued to eat and to growth, although not as much as uninfected control animals. No intervention occurred or treatment provided during the course of the mild disease, as it would have rendered the study results meaningless. However, the animals were monitored closely and if more severe clinical signs had developed, such as acute respiratory distress, the animals would have been euthanized.

3. Eight pigs were infected with salmonella bacteria in experiments to identify attenuated strains that could be used in the development of a salmonella vaccine. Pigs developed no more than mild lethargy, loss of appetite and diarrhea, which was characterized by the researcher as transient mild discomfort. The pigs were monitored 4 times a day and if more severe clinical signs had developed, such as dehydration, persistent anorexia or marked lethargy, the animals would have been euthanized.

If I can be of any further assistance in this matter, please do not hesitate to contact me.

Sincerely,

Th[illegible]equired by law (7 USC 2143). Failure to report according to the regulations can result in [illegible]der to cease and desist and to be subject to penalties as provided for in Section 21[illegible]

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 33-R-0122
CUSTOMER NUMBER: 796

FORM APPROVED
OMB NO. 0579-0036

Pfizer Inc
East Lincoln Road
P. O. Box 221
White Hall, IL 62092

NOV 0 1 2004

Telephone:

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

FACILITY LOCATIONS ( Sites ) - ~~See Atached Listing~~ Given in address, above.

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

| A. Animals Covered By The Animal Welfare Regulations | B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | 2465 | | 390 | 2855 |
| 7. Hamsters | | | | | |
| 8. Rabbits | | 1330 | | | 1330 |
| 9. Non-human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | 69 | | | 69 |
| 12. Other Farm Animals | | | | | |
| Cows | 2 | 189 | | 118 | 307 |
| 13. Other Animals | | | | | |
| Goats | | 9 | | | 9 |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc 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 )

NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL ( Type or Print )

DATE SIGNED
29Oct04

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

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## 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: 33-R-0122

2. Number 118 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

(b)(4)

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)

(b)(4)

All animals recovered.

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 N/A CFR

## 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: 33-R-0122

2. Number 390 of animals used in this study.

3. Species (common name) Guinea pigs of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Non vaccinated animals were challenged with a dose of a clostridium species (chauvoei or haemolyticum) that will cause death.

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)

This procedure is conducted as a potency test for licensed vaccine. Death must be observed in at least 80% of the challenged controls for the test to be considered valid.

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 APHIS CFR 9 CFR 113.106, 113.107

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. 42-R-0009 CUSTOMER NO. 1578

FORM APPROVED OMB NO. 0579-0036

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

FORT DODGE LABORATORIES
800 5TH ST NW
FORT DODGE, IA 50501
(515) 955-4600

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)*

See Attached Listing

800 5th Street NW, Fort Dodge, IA 50501

2000 Rockford Road, Charles City, IA 50616

2973 Highway 18 East, Charles City, IA 50616

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 | 188 | 592 | 2 | 0 | 594 |
| 5. Cats | 0 | 1,031 | 0 | 86 | 1,117 |
| 6. Guinea Pigs | 0 | 4,575 | 0 | 160 | 4,735 |
| 7. Hamsters | 0 | 13,313 | 0 | 6,252 | 19,565 |
| 8. Rabbits | 0 | 435 | 983 | 0 | 1,418 |
| 9. Non-Human Primates | 0 | 0 | 0 | 0 | 0 |
| 10. Sheep | 0 | 0 | 0 | 0 | 0 |
| 11. Pigs | 0 | 15 | 0 | 0 | 15 |
| 12. Other Farm Animals | | | | | |
| Cattle | 0 | 124 | 0 | 0 | 124 |
| 13. Other Animals | | | | | |
| Horses | 2 | 4 | 0 | 0 | 4 |
| | | | | | |
| | | | | | |

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)

(b)(6), (b)(7)(C)

DATE SIGNED
20 Nov 03

ADQUARTERS

COPY

FEB 24 2004 NOV 26 2003

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species: Hamster**

2. **Number of animals achieving Cat. E in this study: 6117**

3. **Explanation of the procedure producing pain and/or distress**

Ten hamsters per serial are vaccinated with 0.25mL given IM. After 14-21 days (product dependent), the hamsters are challenged intraperitoneally (IP) with an appropriate dilution of live leptospira preparation. Ten non-vaccinated hamsters are given the same challenge dose and used as controls. Four groups of five non-vaccinated hamsters are given a dilution of the challenge material and used as the challenge titration determination. Hamsters are observed for 14 days, deaths recorded.

4. **Scientific justification why pain and/or distress could not be relieved.**

The test is required by regulation as a proof of Leptospiral vaccine potency to be conducted on each serial of vaccine produced. Death of hamsters in this test has been used for many years to indicate lack of protection form leptospirosis. Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. Leptospirosis in hamsters almost always results in acute onset and rapid death. The rapid progression of the disease in the hamster gives little opportunity for intervention. Furthermore, pathology would likely be impacted by use of anti-inflammatories. For this reason, neither FDAH nor USDA CVB-L uses any substance to reduce pain or distress. The impact on length of disease, duration and severity, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate (according to Dr. Paul J. Hauer, USDA-CVB-LPD-private communication) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test itself useless for judging vaccine potency.

APHIS-USDA-CVB is engaged in developing in-vitro potency test alternatives for products that require this test and FDAH has been one of the most active industry partners in this effort. Until such time as a validated USDA-CVB approved alternative is available, the standard test is obligatory. No alternatives exist at this time, and no CVB-approved means of relieving pain and distress for this use of hamsters are yet available. When the alternatives are available to a commercially applicable scale, FDAH will apply them.

In 2004 FDAH will be evaluating if intervening prior to death due to the infection for the relief of suffering will affect the outcome of the testing. If no fundamental results are changed, an application to amend the Outline of Production will be made in 2005.

5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**
9CFR 113.01, 113.02, 113.03, 113.04 and USDA approved Special Outline 1117 requires this testing be done in the manner described.

FEB 24 2004

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species: Hamster**

2. **Number of animals achieving Cat. E in this study: 117**

3. **Explanation of the procedure producing pain and/or distress**

Ten hamsters are vaccinated with 0.2mL IM of test vaccine. Thirty hamsters are held for use as controls during the challenge. At 21DPV$_1$, all vaccinated hamsters are challenged intraperitoneally (IP) with 0.1mL of a proper dilution of challenge material. Ten non-vaccinated hamsters are challenged IP with 0.1mL of the same dilution and used as challenge controls. Four groups of five non-vaccinated hamsters are given 0.1mL of diluted challenge (to be used as a challenge titration determination.) All hamsters are observed for 7 days and deaths are recorded.

4. **Scientific justification why pain and/or distress could not be relieved.**

. Death as an endpoint is the current standard and a necessary part of a valid test as determined by USDA approved Outline of Production VS Code 1525.21. Because the challenge is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. Furthermore, pathology and the clinical expression of (b)(4) would likely be impacted by use of anti-inflammatories. The impact on length of disease, duration and severity, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate (according to Dr. Paul J. Hauer, USDA-CVB-LPD- telephone communication) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test itself useless for judging vaccine potency without a validated protective dose and challenge dose being determined.

Until such time as a validated USDA-CVB approved alternative is available, the test is obligatory. No alternatives exist at this time, and no CVB-approved means of relieving pain and distress for this use of hamsters are yet available. When the alternatives are available to a commercially applicable scale, FDAH will apply them.

In 2004 FDAH will be evaluating if intervening prior to death due to the infection for the relief of suffering will affect the outcome of the testing. If no fundamental results are changed, an application to amend the Outline of Production will be made in 2005.

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species: Hamster**

2. **Number of animals achieving Cat. E in this study: 18**

3. **Explanation of the procedure producing pain and/or distress:**

The purpose of this study was to prepare a source of and increase the virulence of (b)(4) challenge material by growing the organism in hamsters. In-vitro culture of (b)(4) reduces the virulence of the organism to an unsatisfactory level. This material is necessary for the development of a new vaccine. The hamsters were inoculated by an intraperitoneal injection of (b)(4) cultured in the laboratory. When the hamsters become sick they were euthanized and the liver was harvested under sterile conditions. The liver will contain (b)(4) with an enhanced ability to cause disease. The liver (after processing) will be used as a source of challenge material for (b)(4)
(b)(4)

4. **Scientific justification why pain and/or distress could not be relieved.**

It is the intent of this study was to increase the virulence of (b)(4) by the replication of the organism in hamsters. The hamsters are euthanized as soon as they display signs of illness. Administration of palliative medication will obscure the clinical presentation of the disease process and will interfere with the researcher's ability to determine when humane euthanasia is warranted. The peracute mortality of hamsters infected with (b)(4) usually precludes euthanasia.

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species: Guinea Pig**

2. **Number of animals achieving Cat. E in this study: 160**

3. **Explanation of the procedure producing pain and/or distress:**

Ten guinea pigs are inoculated with 1 ml subcutaneously with dilutions of tetanus toxin prior to the toxin being inactivated to determine the Minimum Lethal Dosage (MLD) . The animals are observed for five days and signs of paralysis and other symptomology resulting from tetanus are documented. Animal deaths are also recorded

4. **Scientific justification why pain and/or distress could not be relieved.**

Clinical signs and death are the current standard and a necessary part of a valid test as per USDA approved Outline of Production VS Code 8601.01. This test is used to titrate tetanus stock prior to inactivation for downstream processing. The impact on length or severity of signs, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate the scientific value of the protection endpoint determined by the test

FDAH is currently evaluating if an available in-vitro method can be used as the sole method for determining the level of tetanus toxin in production stocks. If no fundamental results are changed, an application to amend the Outline of Production will be made in 2005 with the removal of this use of animals in testing for production purposes.

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species:** Cat

2. **Number of animals achieving Cat. E in this study:** 24

3. **Explanation of the procedure producing pain and/or distress:**
Cats were inoculated under anesthesia, with a virulent strain of (b)(4) (b)(4) known to cause the clinical disease.

4. **Scientific justification why pain and/or distress could not be relieved.**
This animal use was done in the licensing process for new animal vaccines. This research test must be done to the same standards that will apply to the virus challenge test as outlined in (b)(4) stating that controls are required to have white cell counts less than 25% of normal. Therapeutic treatments for symptoms of pain or distress can affect the immune system, thus preventing the required clinical signs associated with (b)(4) (b)(4)

5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

(b)(4) Clinical signs of (b)(4) shall include a pronounced (b)(4) wherein the white blood cell count drops to 4,000 or less per cubic mm or the white cell count drops to less than 25 percent of the normal level established by an average of three or more counts taken prior to challenge.

VS Memorandum 800.202 3.6.1 The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement. Any therapeutic medications can alter the outward appearance of the animal and/or the immune system, preventing the measurement of disease in cats.

VS Memorandum 800.202 4.2 The label claim for this product must be determined under the guidelines of the classifications listed in the memorandum.

FEB 24 2004

# Explanation for Column E
# Fort Dodge Animal Health
# Registration # 42-R-0009

1. **Species:** Cat

2. **Number of animals achieving Cat. E in this study:** 62

3. **Explanation of the procedure producing pain and/or distress:**
Cats were inoculated (b)(4) with a virulent strain of (b)(4) (b)(4) of the disease.

4. **Scientific justification why pain and/or distress could not be relieved.**
This study was for the development of a new feline vaccine. Studies are required to evaluate the relevant clinical signs of disease without the use of treatment to establish label claims. Actions that would have relieved pain and/or distress would not allow comprehensive observations of the clinical signs as well as modify the duration and severity of the clinical signs. This would not allow for true and accurate measure of efficacy for products as well as label claims.

5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

(b)(4) Potency of a vaccine is determined by a significant difference in clinical signs between the vaccinates and controls. The relevant clinical signs for (b)(4) need to be determined.

VS Memorandum 800.202 3.6.1 The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement. (A case definition for (b)(4) needed to be determined.)

VS Memorandum 800.202 4.2 The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

FEB 24 2004

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 0180-00A-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 47-R-0010 CUSTOMER NO. 1550

FORM APPROVED OMB NO 0579-0036

# ANNUAL REPORT OF RESEARCH FACILITY

*(TYPE OR PRINT)*

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

SCHERING-PLOUGH ANIMAL HEALTH
21401 WEST CENTER RD
ELKHORN, NE 68022

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)*

| | |
|---|---|
| Schering-Plough Animal Health<br>21401 W. Center Road | Harlan Inc.<br>Bldg. 232, 6056 N, 156th Street |
| Elkhorn, NE 68022 | Omaha, NE 68116 |

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 | 4 | 365 | 10 | 20 | 395 |
| 5 Cats | 0 | 668 | 1 | 16 | 685 |
| 6 Guinea Pigs | 31 | 807 | 226 | 115 | 1,148 |
| 7 Hamsters | 30 | 74 | 0 | 2,810 | 2,884 |
| 8 Rabbits | 0 | 26 | 437 | 0 | 463 |
| 9 Non-Human Primates | 0 | 0 | 0 | 0 | 0 |
| 10 Sheep | 0 | 0 | 0 | 0 | 0 |
| 11 Pigs | 0 | 0 | 0 | 0 | 0 |
| 12 Other Farm Animals | 0 | 0 | 0 | 0 | 0 |
| | | | | | |
| 13 Other Animals | | | | | |
| Mink | 0 | 289 | 0 | 42 | 331 |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) *Professionally acceptable standards governing the care treatment, and use of animals, including appropriate use of anesthetics, 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)

| SIGN. NAL OFFICIAL | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)* | DATE SIGNED |
|---|---|---|
| | | 11/21/01 |

APHIS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

# 2001 ANNUAL REPORT OF RESEARCH FACILITY

Schering-Plough Animal Health Corp.
21401 West Center Road
Elkhorn, Nebraska 68022

Registration No. 47-R-0010

Column E Entries

I. Dogs:

A total of 20 dogs are listed in Column E. All these dogs were part of a bacterial vaccine challenge development model study conducted according to European Union Council Directive for product registration 92/18/EEC, Part 7, C (1), C (2) and C (3). Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge

II. Cats:

A total of 16 cats are listed in Column E.

Seven cats were used in a dose titration study for a viral vaccine. The study was conducted in accordance with APHIS/VS General Licensing Considerations #800.200 (01 Feb 2000). Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge

Nine cats were part of a dose titration study for another viral vaccine. The study was conducted in accordance with APHIS/VS General Licensing Considerations #800.200 (12 May 1995), APHIS/VS Memorandum (b)(4)
European Union Monograph (b)(4) Directive 92/18/EEC, Title II, Parts 8 & 9; and Guidelines.

III. Guinea Pigs:

A total of 115 guinea pigs are listed in Column E. The guinea pigs were used in six bacterial vaccine potency tests according to APHIS, 9CFR section 113.106. While all the vaccinated animals were protected from death, the nature of the challenge material induced swelling and pain at the injection sites for the duration of the three-day study.

2001 ANNUAL REPORT OF RESEARCH FACILITY

Schering-Plough Animal Health Corp.
21401 West Center Road
Elkhorn, Nebraska 68022

IV. Hamsters:

A total of 2810 hamsters are listed in Column E. The hamsters were used in potency tests or challenge passage/preparation for production of a bacterin. Both tests were conducted according to USDA-mandated methods specified in APHIS, 9CFR sections 113.102 and 113.103. These tests require illness or death as the end point. Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge. In the potency test, all survivors are humanely euthanatized at the end of the 14-day observation period. In the challenge passage test, hamsters designated as liver donors and other surviving hamsters are humanely euthanatized as soon as possible.

V. Mink:

A total of 42 mink are listed in Column E. The mink were used as unvaccinated controls or died despite pre-challenge vaccination as part of bacterin-toxoid and virus potency tests conducted according to USDA mandated methods specified in APHIS, 9CFR sections 113.110 and 113.204. Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge. Surviving mink are humanely euthanatized as soon as possible at the completion of a study.

SUMMARY OF EXCEPTION TO THE REGULATIONS AND STANDARDS – WITH EXPLANATION

In one viral dose titration study involving a total of 37 cats, the study director requested changes in sanitizing requirements due to biosafety concerns about the zoonotic virus involved. These changes were approved by the IACUC.

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 21

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY

( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 47-R-0010

CUSTOMER NUMBER: 1550

FORM APPROVED
OMB NO. 0579-0036

Schering-Plough Animal Health
21401 West Center Rd
Elkhorn, NE 68022

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this repor. | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | 0 | 460 | 25 | 21 | 506 |
| 5. Cats | 91 | 498 | 1 | 0 | 499 |
| 6. Guinea Pigs | 16 | 423 | 555 | 78 | 1,056 |
| 7. Hamsters | 109 | 2,819 | 0 | 1,096 | 3,915 |
| 8. Rabbits | 0 | 51 | 273 | 0 | 324 |
| 9. Non-human Primates | 0 | 0 | 0 | 0 | 0 |
| 10. Sheep | 0 | 0 | 0 | 0 | 0 |
| 11. Pigs | 0 | 0 | 0 | 0 | 0 |
| 12. Other Farm Animals | 0 | 0 | 0 | 0 | 0 |
| | | | | | |
| 13. Other Animals | | | | | |
| Mink | 0 | 229 | 0 | 46 | 275 |
| | | | | | |
| | | | | | |

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in 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 )

| SIGNATURE OF C. | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL ( Type or Print ) | DATE SIGNED |
|---|---|---|
| | | 11/21/02 |

APHIS FORM 7023
( AUG 91 )

(Replaces VS FORM 18-23 (OCT 88), which is obsolete.)

# 2002 ANNUAL REPORT OF RESEARCH FACILITY

Schering-Plough Animal Health Corp.
21401 West Center Road
Elkhorn, Nebraska 68022

Registration No. 47-R-0010

Column E Entries

I. Dogs:

A total of 21 dogs are listed in Column E.

Twenty of these dogs were part of bacterial vaccine challenge development model studies conducted according to European Union Council Directive for product registration 92/18/EEC, Part 7, C (1), C (2) and C (3). Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge. These same 20 dogs are listed on both our 2001 and 2002 Annual Reports because the studies overlapped the reporting periods.

One dog was part of an onset of immunity study for a canine combination vaccine conducted according to European Union Council Directive for product registration 2001/82/EC, Annex I Title II, Parts 8 and 9 and EU Ph monograph 01/2002:0964. Pain and distress-relieving drugs are not utilized in this test because they would mask the effects of the virulent challenge.

II. Guinea Pigs:

A total of 78 guinea pigs are listed in Column E. The guinea pigs were used in six bacterial vaccine potency tests according to APHIS, 9CFR section 113.106. While all the vaccinated animals were protected from death, the nature of the challenge material induced swelling and pain at the injection sites for the duration of the three-day study.

IV. Hamsters:

A total of 1096 hamsters are listed in Column E. These hamsters were used in potency tests or challenge passage/preparation for production of a bacterin. Both tests were conducted according to USDA-mandated methods specified in APHIS, 9CFR sections 113.102 and 113.103. These tests require illness or death as the end point. Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge. In the potency test, all survivors are humanely euthanatized at the end of the 14-day observation period. In the challenge passage test, hamsters designated as liver donors and other surviving hamsters are humanely euthanatized as soon as possible.

V. Mink:

A total of 46 mink are listed in Column E. Forty-one of the mink were used as unvaccinated controls or died despite pre-challenge vaccination as part of bacterin-toxoid and virus potency tests. Five of the mink were used to produce material for the challenge model. The tests were conducted according to USDA mandated methods specified in APHIS, 9CFR sections 113.110 and 113.204. Pain and distress-relieving drugs are not utilized in these tests because they would mask the effects of the virulent challenge. Surviving mink are humanely euthanatized as soon as possible at the completion of a study.

cc: Ruth Barker

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 21

See attached form for additional information.

Interagency Report Control No.: 12-04

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 47-R-0010
CUSTOMER NUMBER: 1550

FORM APPROVED
OMB NO. 0579-0036

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

Schering-Plough Animal Health
21401 West Center Rd
Elkhorn, NE 68022

Telephone:

"A" D. WATKINS
04/20/05

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this repor | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | 0 | 502 | 55 | 7 | 564 |
| 5. Cats | 30 | 436 | 0 | 0 | 436 |
| 6. Guinea Pigs | 1 | 414 | 0 | 39 | 453 |
| 7. Hamsters | 197 | 3612 | 333 | 1829 | 5774 |
| 8. Rabbits | 0 | 0 | 350 | 0 | 350 |
| 9. Non-human Primates | 0 | 0 | 0 | 0 | 0 |
| 10. Sheep | 0 | 0 | 0 | 0 | 0 |
| 11. Pigs | 0 | 0 | 0 | 0 | 0 |
| 12. Other Farm Animals | 0 | 0 | 0 | 0 | 0 |
| | | | | | |
| 13. Other Animals | | | | | |
| Ferrets | 0 | 0 | 0 | 15 | 15 |
| Mink | 28 | 193 | 0 | 79 | 272 |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or expenimentation 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 snd explained by the principal investigator and apr Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in 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 )

| SIGNATUR | ICIAL 11/22/04 | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL ( Type or Print ) | DATE SIGNED |
|---|---|---|---|
| | | | |

APHIS FOR
( AUG 1

8-23 (OCT 88) which is obsolete.)

# 2004 USDA ANNUAL REPORT OF RESEARCH FACILITY
# SCHERING PLOUGH ANIMAL HEALTH CORPORATION
## 21401 West Center Road – Elkhorn – NE – 68022
## REGISTRATION #47-R-0010
## Column "E" Entries

I. Dogs:

A total of seven dogs are listed in column E. Two dogs became ill due to a viral challenge as mandated by (b)(4) Pain and distress-relieving medications were not utilized in these tests since they would mask the effects of the virulent challenge. Five dogs became ill following a bacterial challenge. The treatment of the dogs was delayed to evaluate clinical signs for development of a new bacterin as per VS Memorandum 800.202. In both the viral and bacterial challenge the clinical signs were evaluated and recorded carefully to define sensitive endpoints. These sensitive endpoints will be applied to future studies. IACUC has approved all of these studies.

II. Guinea Pigs:

A total of 39 guinea pigs are listed in column E. The guinea pigs were used in *Clostridium chauvoei* bacterin potenency tests. The potency test was performed according to USDA-mandated methods specified in 9 CFR section 113.106 (c) and the guinea pigs experienced illness or local irritation from the *C. chauvoei*. IACUC approved all of these studies, as they are required.

This test is a bacterin potency test required by regulation to be conducted on each serial of bacterin. The effect of pain medications on the length and severity of the disease is not known, and thus would invalidate the scientific value of the potency test (USDA CVB-PEL, private communication). The rapid progress of the disease in guinea pigs gives little opportunity for intervention. Furthermore, the normal progression of the disease would likely be affected by the use of anti-inflammatory medication. For this reason, neither our company, nor the USDA CVB-PEL, uses any substance to reduce pain or distress. APHIS-USDA-CVB is engaged in developing an *in vitro* test as an alternative to the guinea pig test for products that contain *C. chauvoei* fractions (b)(4)

(b)(4)

III. Hamsters

A total of 1829 hamsters are listed in column E. The hamsters were used for Leptospira vaccine potency testing. Tests were conducted according to USDA-mandated methods specified in 9 CFR sections 113.101 (c), 113.102

(c), 113.103 (c), and 113.104 (c), and for this reason, IACUC approved these studies. These tests are potency tests, required by regulation for the release of each bacterin serial. Because the bacterin is given at a fractional dose, the test amounts to a protective endpoint determination for the bacterin being tested.

Pathology would likely be impacted by use of anti-inflammatories. For this reason neither our company nor USDA CVB-PEL uses any substances to reduce pain or distress. The impact on the length of disease, duration, and severity, which might occur with the use of pain medications, is not known. Use of any drugs therefore, would invalidate (according to private conversation with USDA-CVB-PEL) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test useless for judging vaccine potency.

(b)(4)

(b)(4) APHIS-USDA-CVB is engaged in developing in vitro potency test alternative for products that require this test and SPAH has actively participated in this effort. The current test must remain in effect until the CVB approves of a new test and the revised Outline of production.

IV. Ferrets

A total of 15 ferrets are listed in column E. The ferrets were utilized to produce a new lot of challenge virus following a method provided by the Center of Veterinary Biologics. Clinical signs included depression, ocular and nasal discharge, and conjunctivitis. Pain and distress relieving medications were not utilized in these tests since they would mask the effects of virulent challenge such as depression. These effects or clinical signs were closely monitored and utilized as sensitive endpoints. This allowed us to euthanize 14 of the 15 ferrets to minimize suffering following presentation of the clinical signs.

V. Mink

A total of 79 mink are listed in column E. 55 of the mink were used in potency tests for a Clostridium vaccine and 24 were utilized for the production of a new lot of viral enteritis challenge virus. IACUC has approved all of these studies.

The new lot of challenge viral enteritis virus is utilized in the viral enteritis potency test as required by 9 CFR section 113.204 (b). The clinical signs occurred 4-8 days after infection. The clinical signs included anorexia, lethargy, and diarrhea. Pain medication was not utilized to prevent masking

the effects of the virulent challenge such as lethargy. These effects or clinical signs were closely monitored. This allowed us to euthanize 22 of the 24 mink following presentation of the clinical signs to minimize suffering.

Tests for the Clostridium vaccine were conducted according to a USDA-mandated method specified in 9 CFR section 113.110 (c). The Clostridial potency test is required by regulation as a proof of Clostridial vaccine potency to be conducted on each serial of vaccine produced. For the required potency tests, the progression of the disease would likely be affected by the use of anti-inflammatory medications. For this reason, neither our company, nor USDA CVB-PEL, uses any substance to reduce pain or distress. It is not known how the use of pain medications would affect the length and severity of the disease. Therefore, use of these drugs would invalidate (according to private communication with USDA-CVB-PEL) the scientific value of the protection endpoint determined by the test. Lack of confidence in the test would render the test itself useless for judging vaccine potency.

APHIS-USDA-CVB is engaged in developing in vitro potency test alternatives for products that require animal testing for product release. Our company has been an active partner in these efforts. Until validated USDA-CVB approved alternatives are available, the standard tests are obligatory. No alternatives exist at this time.

Exemption of Animal Welfare Act

Twenty (20) dogs on a bacterial study met the minimum space requirements as specified in the Animal Welfare Act. The dogs were also regularly exercised until challenge. However, in order to provide careful observation, avoid cross exposure of the subjects, and for the safety of the staff, the animals remained in their cages for 21 days of the study. This was approved by IACUC.

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 21: NOV 2 3 2004 See attached form for additional information. Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 50-R-0003
CUSTOMER NUMBER: 27

FORM APPROVED
OMB NO. 0579-0036

Intervet Inc
405 State Street
P.O. Box 318
Millsboro, DE 19966

Telephone:

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | 264 | | | 264 |
| 5. Cats | | 401 | 119 | 75 | 595 |
| 6. Guinea Pigs | 13 | 439 | 1145 | 763 | 2347 |
| 7. Hamsters | | 1671 | 116 | 3668 | 5455 |
| 8. Rabbits | 9 | 24 | 1480 | 794 | 2298 |
| 9. Non-human Primates | | | | | |
| 10. Sheep | | 168 | | | 168 |
| 11. Pigs | | 3151 | | | 3151 |
| 12. Other Farm Animals | | | | | |
| Cattle | | 1856 | | | 1856 |
| 13. Other Animals | | | | | |
| Horses | | 261 | | | 261 |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc 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 )

| SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *( Type or Print )* | DATE SIGNED |
|---|---|---|
| | | 11/18/04 |

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

## 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: 50-R0003

2. Number 75 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

   Following challenge animals required for acceptance is death due to rabies challenge with rabies

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 APHIS 9 CFR 113.209 (3) (V)

## 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: 50-R-0003

2. Number 763 of animals used in this study.

3. Species (common name) Guinea Pigs of animals used in the study.

4. Explain the procedure producing pain and/or distress.

All Guinea Pigs were used for testing as specified in 9CFR. All Clinical signs and death are required when inoculated with Clostridium chauvoei.

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 APHIS 9 CFR 113.106, 113.107

## 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: 50-R-0003

2. Number 1629 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

   Qualification of new reference potency. Death is the end point.

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 CVB CFR 113.8 (A) (3) (2)

## 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: 50-R-0003

2. Number 2039 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

   All hamsters were used for testing as stated by 9CFR. Death is the end point.

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 APHIS CFR 113.01, 113.102, 113.103, 113.104, 113.105

## 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: 50-R-0003

2. Number 794 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

   All rabbits (794) were challenged with Clostridum Septicum. Pain and distress are due to the disease processes associated with the challenge. Animals are allowed to go 72 hours, when test results are interpreted.

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 CVB 9 CFR 133.5

DEC 04 2002

This report is required by law (7 U.S.C. 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-AM

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

**1. CERTIFICATE NUMBER:** 57-R-0003
**CUSTOMER NUMBER:** 896

FORM APPROVED OMB NO. 0579-0036

**2. Headquarter Research Facility** *(Name and address, as registered with USDA.)*
Emory University
1440 Clifton Road, NE
Atlanta, GA 30322

Telephone: (404) 727-7428

**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*)

| | |
|---|---|
| See Attached | |
| | |

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

| A. 2002 Animals Covered By the Animal Welfare Regulations | B. 2002 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. 2002 Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs. | D. 2002 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. 2002 Number of animals upon which teaching, experiments, research, surger 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. 2002 TOTAL NO. OF ANIMALS (Cols. C + D + E) |
|---|---|---|---|---|---|
| 4. Dogs | 0 | 52 | 138 | 0 | 190 |
| 5. Cats | 0 | 0 | 84 | | 84 |
| 6. Guinea Pigs | 0 | 30 | 70 | | 100 |
| 7. Hamsters | 0 | 0 | 0 | | 0 |
| 8. Rabbits | 0 | 181 | 111 | 4 | 296 |
| 9. Non-human Primates | 1261 | 341 | 2322 | 17 | 2680 |
| 10. Sheep | 0 | 7 | 19 | | 26 |
| 11. Pigs | 0 | 0 | 292 | | 292 |
| 12. Other Farm Animals | | | | | 0 |
| | | | | | 0 |
| 13. Other Animals | 0 | 638 | 51 | | 689 |
| | | | | | |

**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 such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, th 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 adequecy 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 | DATE SIGNED |
|---|---|---|
| | | |

**APHIS FORM 7023**
(AUG 91)

Rec

**Annual Report to USDA**
**Facility Locations**

Peavine Creek Kennels, Emory University
O. Wayne Rollins Research Center, Emory University
Woodruff Memorial Research Building, Emory University
Wesley Woods, Emory University
Dental Building, Emory University
South Clinics (Winship Cancer Center and Eye Center), Emory University
Cell Biology Building, Emory University
Physiology Building, Emory University
Grady Memorial Hospital, Woodruff Extension, Atlanta, GA
Briarcliff Campus Building, Emory University
Cardiothoracic Research Labs at Crawford Long Hospital, Atlanta, GA
Yerkes Regional Primate Research Center, Emory University
Yerkes Field Station, Lawrenceville, GA
Whitehead Memorial Research Building, Emory University

## Summary of Studies (Animal) Listed in Column E

Title: Behavioral Pharmacology of Narcotic Antagonists

- 17 squirrel monkeys

Squirrel monkeys are used in drug discrimination studies for studies of in the brain. In these studies, opioid drugs with differing or unknown profiles of receptor interactions are evaluated. The objective is to identify and study those components of drug action that underlie potential for abuse. It should be noted that an alternative species, rats, is used for most of these studies and squirrel monkeys are involved to a lesser extent.

Squirrel monkeys are trained to discriminate between a reference drug, such as Monkeys are loosely seated in a primate chair during these studies. During the training phase and as an aversive stimulus to respond during discrimination trials, a 0.5-1.0 second mild electrical stimulus may be delivered to the monkey's tail after 5 seconds from the beginning of the trial. The monkeys can terminate the trial and prevent the electrical shock by pushing on one of two levers (corresponding to the reference drug or the placebo). The monkeys quickly learn to avoid the stimulus by responding during the five seconds after the start of the trial. After the initial training session, the monkeys rarely, if ever, receive an electrical stimulus. Shocks are never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the shock.

Pain-relieving drugs are not used in these studies because any pain experienced will be transient (one second or less) and the animal can take action to avoid all pain (by pushing a lever within 5 seconds of a clear cue). Additionally, pain-relieving drugs, such as narcotics, will confound the pharmacological effects of the opioid compounds studied.

Title: Oxidative Hypothesis – Paradoxes and Pitfalls

- 4 rabbits

Rabbits are by subcutaneous injection using a refined procedure that minimizes or eliminates clinically apparent distress by limiting the quantity of given and using small volumes per injections site. However, analgesic agents are not given because of concern that the immune response necessary to elicit antibody production may be impaired.

## Exceptions to Regulations and Standards

Exemptions from Social Enrichment for Nonhuman Primates: Short-term Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by Monkeys are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. These monkeys may be maintained in the observation and recording room for a maximum of 7 days and are then returned to their home cage in a colony with other monkeys of the same species. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with which telemeter This telemetric approach allows studying sleep behavior in monkeys that are unrestrained.

In another movement disorder study, monkeys are housed in a specially arranged isolation room for 72 hours after each administration of Although this is a transient, post-operative care housing situation, the animals will be repeatedly isolation-housed. Whenever possible, an already -lesioned monkey will be housed with the recently injected monkey in order to provide visual, auditory and olfactory contact with a conspecific. It is understood that the stress of short-term room changes on a monkey may be a greater than the stress of isolation housing would be for the recently -injected subject, so housing will be evaluated on a case-by-case basis. In the extremely low-dose protocol, with dosing occurring every 2-3 days, the need to house the subject away from other monkeys will be constant. Therefore, the short-term stress of room changes is unlikely to outweigh the benefits to the subject undergoing MPTP dosing.

- State dependent motor control in neurologic disease: 4 rhesus monkeys
- Glutamate in Parkinson's disease: 7 rhesus macaques
    - Study involves administration of

Exemptions from Social Enrichment for Nonhuman Primates: Single-housing in Sight and Sound of Conspecifics

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Experiments to test whether i

During a period of 4-8 months, subjects will have indwelling venous catheters; protected contact housing is required during this period to avoid removal of catheters by cagemates.

- Growth regulation of the neurobiology of puberty: 85 rhesus monkeys

B. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

Another study is being done to establish a pregnant rhesus monkey animal model for human Listeria infection and to develop methodology for determining dose information to be used in a risk assessment for Listeria monocytogenes. Single caging is required during the time between infection and one month post-delivery primarily to prevent transmission of the *Listeria* organism from experimentally infected animals to non-infected animals, as well as to permit the collection of fecal samples from the experimentally infected animal to check for fecal shedding of *Listeria* organisms. If infants are liveborn, they are returned to their mothers following testing.

A study testing the effects of requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Other related studies are looking at uses to express and switch expression of the variant antigen at the surface of the infected red blood cell and the relationship of malaria to anemia in pregnant women. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period of treatment in a hepatitis C suppression study, it is necessary to maintain the animals in metabolism cages. This is due to the twice daily drug administration and frequent blood collections.

- Core A: Preclinical trials and pathology (Part of NCVDG Grant: DNA and protein immunogens for SIV/HIV vaccines): 63 Rhesus macaques
- New live viral vectors in candidate AIDS vaccines: animal trials core: 2 chimpanzees, 16 rhesus macaques
- Cellular immune responses and AIDS pathogenesis: 7 rhesus macaques and 7 mangabeys
- Core A: Nonhuman primates (Part of program project grant entitled: DNA/MVA immunogens, cross-clade immune responses): 42 rhesus macaques
- Induction of P vivax, P ovale, P malariae and other plasmodium infections in chimpanzees to obtain large volumes of parasites for malaria vaccine studies: 6 chimpanzees
- Generation and recovery of plasmodium falciparum liver stage parasites in chimpanzees: 2 chimpanzees
- Molecular evolution of multiply deleted SIV in vitro: 34 rhesus macaques
- Core C: Primate Studies: 22 rhesus macaques
- Fetal immunoprophylaxis against a primate lentivirus: 22 rhesus macaques
- Development of a risk assessment dose-response model for foodborne listeria: 22 rhesus macaques
- Mechanism of oral SIV transmission: 11 rhesus macaques
- Analysis of thymic function during SIV infection: 6 mangabey, 1 rhesus macaque
- Modified nucleosides for HCV: 2 chimpanzees
- T cell turnover in normal and SIV infected sooty mangabeys: 8 mangabeys, 1 rhesus
- SHIV macaque model of oral immunization against sexually transmitted HIV: 8 rhesus/pigtail macaques
- Replication defective HIV vaccine: 7 rhesus macaques
- Impact of anti-CD8 antibody treatment on viral dynamics in SIV-infected sooty mangabeys: 12 mangabeys
- CNS as a viral reservoir in SIV infected macaques: 1 rhesus macaque
- Oral transmission of SIV in neonatal and adult macaques: 12 rhesus macaques
- Role of virus specific immunity in primate AIDS: 3 mangabeys, 7 macaques
- Molecular analysis of antigenic variation in malaria: 19 rhesus macaques
- Malaria, pregnancy and immunophysiopathology: 4 rhesus macaques
- In vivo evaluation of candidate drugs: 12 rhesus macaques
- AIDS & opiates: a monkey model: 29 rhesus macaques
- Determinants of HIV/SIV mucosal transmission: 9 rhesus macaques
- Combination DNA and attenuated virus vaccine for SIV : 14 pigtail macaques
- Immune modulation of neurotropin in SIV infection: 14 rhesus macaques

C. Lumbar spine fusion is commonly performed in humans, but the failure to achieve a solid bone union is reported 10-40% of the time. The required doses of bone growth factors, which have enhanced bone formation in lower vertebrates, are much higher in humans. If these bone growth factors were successful in humans, it could improve the frequency of healing success, decrease healing time and decrease pain in patients. Therefore, studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for

human clinical trials. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Animals receiving adenovirus will be housed singly for 3 days after surgery to insure that viral shedding does not adversely affect other animals or humans. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

- Use of osteoinductive factors to enhance spine fusion: 30 rhesus macaques

D. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One research application involves biochemical mechanisms underlying the effectiveness of olanzapine in treating human schizophrenic patients. Another is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have an indwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery, craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

- Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
- Medications for drug abusers: 17 Squirrel monkeys
- Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 20 Rhesus macaques
- Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
- Effects of Olanzapine on extracellular monoamines in rhesus monkeys: 8 rhesus macaques
- Cortical circuitry related to neurotransmission proteins: 3 rhesus macaques

E. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye

movements as humans. To facilitate the research, scleral search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

- Neural control of visual vestibular behavior: 18 rhesus macaques

F. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and (b)(4) are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. Therefore, animals receiving an arterial graft are housed singly for 21 days after abdominal surgery to allow daily postoperative monitoring.

- Hematopoietic chimerism and transplant tolerance: 11 rhesus macaques
- Non-human primate pancreatic islet cell transplantation: 12 rhesus macaques
- The effect of dosing strategy for LEA29Y on renal allograft survival in rhesus macaques: 2 rhesus macaques
- Activation, apathy, anergy, and apoptosis in transplantation: 41 rhesus
- CD45RB and kidney transplantation: 9 rhesus macaques
- Dose effect of busulfan in the primate model: 2 rhesus macaques
- Transplant Tolerance in Non-Human Primates: Costimulation, chimerism and tolerance in transplantation (Project 3): 11 rhesus macaques
- Transplant tolerance: costimulation, cytokines and chimerism (Project 3: costimulatory blockade and chimerism tolerance): 26 rhesus macaques

G. Cardiovascular disease remains the leading cause of mortality in Western societies. Blood flow to critical vascular beds become stopped or reduced, leading to heart attacks and strokes. Surgical replacement of diseases arteries with artificial substitutes has worked moderately well for larger vessels, but has been problematic for replacing smaller diameter vessels (less than 6mm i.d.) Specific and effective molecular level therapies may represent a promising strategy. In this study, subjects will have carotid artery graft implants , aorto-iliac graft implants, and aortic interposition grafts. Protected contact housing is required for 7-10 days to protect surgical sites. The remaining time, animals will be group housed. Another study will be looking at probes that interfere with thrombogenesis (activation of blood

coagulation, inhibition of platelet activation and inhibition of platelet attachment to injured blood vessel walls). Animals are singly housed to permit repeated access for blood sampling and noninvasive imaging procedures and to protect the surgical access site.

- Evaluation of small vessel prostheses: 34 baboons
- In vivo platelet interactions with adhesive glycoproteins: 28 baboons

H. Some of the animals used under these conditions are in studies of normal control of movement or motion disorders. Monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Administration of the neurotoxin to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given ire generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.
   - Dystonia in cebus monkeys: 2 capuchin monkeys
   - Muscle re-assembly in MI during skill acquisition: 2 rhesus macaques
   - Therapeutic role of subthalamic nucleus activation: 5 rhesus monkeys
     - Study involves administration of
   - Glutamate in Parkinson's disease: 7 rhesus macaques
     - Study involves administration of
   - A novel model of Parkinson's disease: 1 rhesus macaque

Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson's Disease (PD) because of the great similarity of brain function and that Monkeys in these studies usually are given by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, single housing is only done for a 3 day period immediately after administration of during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction – otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair or face-mask cage and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

In a study looking at (b)(4) changes in neurochemistry, monkeys will be seated in a standard primate restraint chair. Probes will be inserted bilaterally into the guide cannulae and connected to infusion equipment. The experimental perfusion lasts 5 hours. Animals will typically spend time in the chair 2-3 days per week.

For the evaluation of small vessel prostheses, animals will be immobilized for a short duration with (b)(4) administered IM. This is augmented by oxygen + isoflurane if needed.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks.

These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet. In one study, monkeys under 6 months of age have their heads immobilized with Velcro straps. After 6 months, a small, light-weight aluminum halo, of the type used in patients with neck injuries, to fix the head to the chair. Between 6 and 12 months of age, the halos will be removed every 2 weeks for at least 1 week. The duration of the testing sessions is gradually increased from 10-15 minutes to an hour over the course of the first two weeks and up to 3 hours over the course of 3 months. Behavioral training occurs up to five times per week. At any sign of distress (e.g., wiggling in the chair or vocalization) the session is terminated.

Monkeys in these studies have transiently-induced movement disorders and are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or restricted, but provided during and after laboratory testing sessions, and with short-term periods of restraint:

    - The substantia nigra in movement and movement disorders: 9 rhesus monkeys
    - Influence of subthalamic nucleus on striatal dopamine: 3 rhesus monkeys
    - Pathophysiology of the basal ganglia in Parkinsonism: 4 rhesus monkeys
    - Cortical mechanisms of motor processing: 3 rhesus monkeys
        - Study does not involve MPTP
    - Development of gaze-holding abilities: 8 rhesus macaques
    - Neural control of visual vestibular behavior: 18 rhesus macaques
    - A novel model of Parkinson's disease: 1 rhesus macaque
    - The error signal for postnatal eye growth in the primate: 7 rhesus macaques

2. Short-term physical restraint only:
    - Basal ganglia pathophysiology in dystonia monkeys: A pilot study: 1 capuchin monkey

- Glutamate in Parkinson's disease: 7 rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 20 rhesus macaques
- Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
- Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
- Effects of (b)(4) on extracellular monoamines in rhesus monkeys: 8 rhesus macaques
- In vivo platelet interactions with adhesive glycoproteins: 28 baboons
- Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
- Does brain oxytocin mediate social interactions between juvenile male Macaca mulatta: 31 rhesus macaques
- Evaluation of small vessel prostheses: 34 baboons
- Gene profiling in drug addiction in nonhuman primates: 4 rhesus macaques
- Medications for drug abusers: 17 squirrel monkeys

Food or Water Restriction of Dogs

Following gastric by-pass surgery, dogs are not fed for four days to permit uneventful healing of the stomach. Intravenous fluids are given to maintain hydration. Dietary transition is then done to a soft diet and subsequently to feeding conventional canine diets. Providing fluid needs are met, well-nourished animals easily tolerate several days without food. Current veterinary standards dictate that postoperative fasted animals not be subjected to the risk associated with parenteral administration of nutrients (JAVMA 201: 699-73, 2000).

- Helicobacter pylori infection of the excluded stomach after gastric bypass: 5 dogs

Exemptions from Exercise for Dogs – none

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

1. REGISTRATION NO. 74-R-0011 CUSTOMER NO. 1382

FORM APPROVED OMB NO 0579-0036

# ANNUAL REPORT OF RESEARCH FACILITY

*(TYPE OR PRINT)*

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

ALCON RESEARCH, LTD
6201 S FREEWAY
FORT WORTH, TX 76134

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)*

See Attached Listing

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 | | | | | |
| 5 Cats | | 20 | | | 20 |
| 6. Guinea Pigs | 2 | 7 | 706 | 4 | 717 |
| 7. Hamsters | | | | | |
| 8. Rabbits | 259 | 1,728 | 3,367 | | 5,095 |
| 9 Non-Human Primates | 85 | | 258 | | 258 |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

RECEIVED
NOV 14
USDA, APHIS, PPQ, AC
SACRAMENTO, CA

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 |
|---|---|---|
| | | 11-02-01 |

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

PART 1 - HEADQUARTERS

**APHIS Form 7023 Site List**

The following sites have been reported by the facility.

---

Registration Number: 74-R-0011
Customer Number: 1382
Facility: ALCON RESEARCH, LTD
6201 S FREEWAY
FORT WORTH, TX 76134

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SITE1
6201 SOUTH FREEWAY
FORT WORTH, TX 76134

Site 2
Dallas Veterans Affairs Medical Center
4500 S. Lancaster Road
Dallas, TX 75216

Telephone:

## 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: 74-R-0011

2. Number 8 total/4 in Column E of animals used in this study.

3. Species (common name) guinea pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

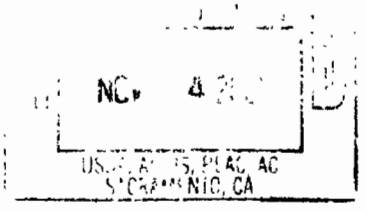
Guinea pigs are injected with approximately 0.06% sodium hyaluronate, horse serum (positive control), or 0.9% saline (negative control), on three occasions into the peritoneal cavity. Subsequently, each test subject is injected intravenously and examined for anaphylactic response for a period up to 23 days. Guinea pigs are humanely euthanized after the last regimen is completed. The 4 animals in Column E are postive controls and are expected to exhibit symptoms of respiratory distress, collapse, and death.

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)

The guinea pig is an established model for antigen-induced respiratory anaphylaxis. Anaphylaxis is the required outcome of the positive control for this study. No analgesic compounds were administered since they would potentially confound interpretation and conclusions from this study. This test was developed in response to required safety testing by the Japanese Ministry of Health and Welfare for marketing viscoelastic products in Japan.

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 Japanese Ministry of Health and Welfare CFR The Pharmacopoeia of Japan, 13th edition, 1996, page 322



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.** 74-R-0050 **CUSTOMER NO.** 1481

FORM APPROVED
OMB NO 0579-0036

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

TEXAS TECH UNIVERSITY HSC
3601 4TH ST
LUBBOCK, TX 79430
(806) 743-2565

Laris

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)*

See Attached Listing

**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 | | 3 | 24 | | 27 |
| 5 Cats | | | 72 | | 72 |
| 6 Guinea Pigs | | | 6 | | 6 |
| 7. Hamsters | | 159 | 31 | 60 | 250 |
| 8. Rabbits | | 248 | 48 | | 296 |
| 9. Non-Human Primates | | | 14 | | 14 |
| 10. Sheep | | | | | |
| 11. Pigs | | | 21 | | 21 |
| 12 Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| Deer Mice | | 93 | | | 93 |
| Prairie Voles | | 27 | | | 27 |
| | | | | | |

**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

NOV - 5 2001

**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 |
|---|---|---|
| | | 10/29/01 |

**APHIS FORM 7023** (AUG 91) **(Replaces VS FORM 18-23 (Oct 88), which is obsolete** School of Biomedical Sciences **PART 1 - HEADQUARTERS**

**APHIS Form 7023 Site List**

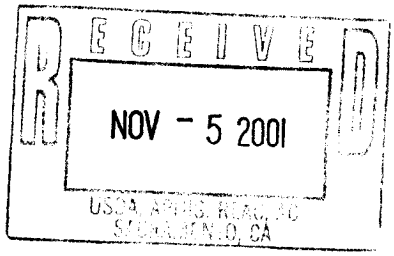
The following sites have been reported by the facility.

| | |
|---|---|
| Registration Number: | 74-R-0050 |
| Customer Number: | 1481 |
| Facility: | TEXAS TECH UNIVERSITY HSC<br>3601 4TH ST<br>LUBBOCK, TX 79430<br>(806) 743-2565 |

SITE1
3601 4TH ST.
LUBBOCK, TX 79430

SITE 2
4800 ALBERTA DR
EL PASO, TX 79905

SITE 3
1400 WALLACE BLVD
AMARILLO, TX 79105



## 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: 74-R-050

2. Number 60 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

Each hamster will be administered (b)(4)

(b)(4)

(b)(4)

Observed at least every (b)(4)

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)

Only live animals can be used to demonstrate prevention of a disease development. Analgesics cannot be administered because they will inhibit some of the pathology (e.g. inflammation) we are attempting to define in this animal model.

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 _____

TEXAS TECH
UNIVERSITY
HEALTH SCIENCES CENTER

Laboratory Animal Resources Center

3601 4th Street
BC101 HSC Bldg.
Lubbock, TX 79430
(806) 743-2565
FAX (806) 743-1028

October 29, 2001

Robert M. Gibbens, DVM
Regional Director, Animal Care
Western Regional Office
U.S. Department of Agriculture
9580 Micron Avenue, Suite J
Sacramento, CA 95827

RE: Registration # 74-R-050
Annual Report of Research Facility

Dear Dr. Gibbens:

Attached is the Annual Report of Research Facility for the Texas Tech University Health Sciences Center.

This report represents the composite activity of all four sites listed under Facility Locations and on the Application for Registration dated March 29, 1996.

We trust this Annual Report will fulfill our reporting obligations for the period October 1, 2000 through September 30, 2001.

Sincerely yours,

2277
7/21/04

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.** 84-R-0051 **CUSTOMER NO.** 1273

FORM APPROVED
OMB NO. 0579-0036

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

GENESIS LABORATORIES, INC.
10122 N.E. FRONTAGE ROAD
WELLINGTON, CO 80549
(970) 568-7059

**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)*

See Attached Listing

**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 | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | 5 | 60 | 0 | 0 | 60 |
| 7. Hamsters | | | | | |
| 8. Rabbits | | | | | |
| 9. Non-Human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| Wild Norway Rat | 39 | 43 | 0 | 64 | 107 |
| Wild House Mouse | 0 | 9 | 0 | 15 | 24 |
| Plains Pocket Gopher | 16 | 26 | 0 | 0 | ~~42~~ 26 |

per ltr dated 7/16/04 mc

**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 |
|---|---|---|
| | | 11-26-03 |

**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

**1. REGISTRATION NO.** 84-R-0051 **CUSTOMER NO.** 1273

FORM APPROVED
OMB NO. 0579-0036

# CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

*(TYPE OR PRINT)*

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

GENESIS LABORATORIES, INC.
10122 N.E. FRONTAGE ROAD
WELLINGTON, CO 80549
(970) 568-7059

**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) |
|---|---|---|---|---|---|
| Mexican Woodrat | 0 | 61 | 0 | 0 | 61 |
| White-footed Mouse | 85 | 0 | 0 | 0 | 0 |
| Rock Squirrel | 0 | 40 | | 4 | 44 |
| Black-Tailed Prairie Dog | 0 | ~100① | 0 | 0 | 100 |
| Eastern Mole | 0 | 0 | 0 | 9 | 9 |
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| | | | | | |
| ① Field Study. This is estimated number of animals on plot. | | | | | |

**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 |
|---|---|---|
| | | 11-26-03 |

**APHIS FORM 7023A** (AUG 91)

**(Replaces VS FORM 18-23 (Oct 88), which is obsolete**

**PART 1 - HEADQUARTERS**

ANNUAL REPORT OF ANIMALS USED BY GENESIS LABORATORIES, INC.
DURING THE 12 MONTH PERIOD OCTOBER 1, 2001 TO SEPTEMBER 30, 2003

| HEADQUARTERS OF RESEARCH FACILITY | FACILITY LOCATIONS |
|---|---|
| GENESIS LABORATORIES, INC.<br>10122 N. E. FRONTAGE ROAD<br>WELLINGTON, COLORADO 80549<br>Registration # 84-R-051 | GENESIS LABORATORIES, INC.<br>10122 N. E. FRONTAGE ROAD<br>WELLINGTON, COLORADO 80549<br>Registration #: 84-R-051 |

The explanations contained in this report were approved by the Genesis Laboratories, Inc, IACUC committee.

ANIMALS REPORTED IN COLUMN E

**Wild Norway Rat (*Rattus norvegicus*)**

Sixty four (64) rats used were from column E in the Annual Report. All animals used were used in studies testing rodenticides. USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-10, Commensal Rodents, was followed during these procedures. FIFRA mandates that efficacy data be generated to support label claims for Norway rat control. For rodenticide efficacy studies, no appropriate anesthetic, analgesic, or tranquilizing drugs were used to relieve the pain. There are no alternatives available to this painful procedure. Logic dictates that the only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

**Wild House Mouse (*Mus musculus)***

Fifteen (15) mice used were from column E in the Annual Report. All were used for product efficacy testing of rodenticides. USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-10, Commensal Rodents, was followed during these procedures. FIFRA mandates that efficacy data be generated to support label claims for house mouse control. For rodenticide efficacy studies, no appropriate anesthetic, analgesic, or tranquilizing drugs were used to relieve the pain. There are no alternatives available to this painful procedure. Logic dictates that the only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

**Rock Squirrel (*Spermophilus variagatus*)**

Four (4) rock squirrels used were from column E in the Annual Report. All were used for product efficacy testing of a rodenticide. USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-12, Field Rodents, was followed during these procedures. FIFRA mandates that efficacy data be generated to support label claims for squirrel control. For rodenticide efficacy studies, no appropriate anesthetic, analgesic, or tranquilizing drugs were used to relieve the pain. There are no alternatives available to this painful procedure. Logic dictates that the only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

**Eastern Mole (*Scalopus aquaticus*)**

Nine (9) moles used were from column E in the Annual Report. All were used for product efficacy testing of a rodenticide. USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-8, Mole Toxicants, was followed during these procedures. FIFRA mandates that efficacy data be generated to support label claims for mole control. For field efficacy studies, no appropriate anesthetic, analgesic, or tranquilizing drugs were used to relieve the pain. There are no alternatives available to this painful procedure. Logic dictates that the only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for mole control.

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 215

See attached form for additional information.

Interagency Report Control No.: 5117

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY

( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 87-F-0002
CUSTOMER NUMBER: 1211

FORM APPROVED
OMB NO. 0579-0036

U. S. Army Dugway Proving Ground
Life Sciences Division
Cste-Dtc-Dp-Wd-L
Dugway, UT 84022

Telephone: (435) -831-5173

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress In these animals and the reasc such drugs were not used must be attached to this report | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | | | | | |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | | | | |
| 7. Hamsters | | | | | |
| 8. Rabbits | | | | | |
| 9. Non-human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| Nonregulated animals | | | | | |
| Mice | 102 | 12 | | 28 | 40 |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in brief explanation of the exceptions, as well as the species and number of animals affected.

4) Tho 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 )

NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *( Type or Print )*

DATE SIGNED 1/11/07

APHIS FORM 7023 / ( AUG 91 )

(Replaces VS FORM 18-23 (OCT 88), which is obsolete.)

## 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: 87-F-0002

2. Number 28 of animals used in this study.

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

4. Explain the procedure producing pain and/or distress.

Life Sciences Division, Dugway Proving Ground produced (b)(2)High (b)(2)High These materials must be evaluated prior to use for both bioactivity and toxicity. Bioactivity is determined by the "Mouse $LD_{50}$ Assay Model". (b)(2)High are injected into different groups of mice. The endpoint is death. The is determined by the group of mice in which 50% of the animals survive.

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)

(b)(2)High The introduction of into a living mouse can cause distress. Even though the endpoint is death, the principle investigator has attempted to ameliorate the situation by humanely euthanizing any distressed animal. (An euthanized, distressed animal was considered to have died due to the effects of the ). In working with , it is essential from a biosurety and biosafety standpoint to know the bioactivity or lethality of the materials.

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

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 215

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
( TYPE OR PRINT )

1. CERTIFICATE NUMBER: 93-R-0026
CUSTOMER NUMBER: 1182

FORM APPROVED
OMB NO. 0579-0036

S R I International
333 Ravenswood Avenue
Menlo Park, CA 94025

Telephone: (650) -859-2412

AJ 12,404

"A" by K. Garland 02-0405

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

FACILITY LOCATIONS ( Sites ) - See Atached Listing

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

| A. Animals Covered By The Animal Welfare Regulations | B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. ( An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report | F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E ) |
|---|---|---|---|---|---|
| 4. Dogs | 1 | 78 | 3 | 2 | 83 |
| 5. Cats | | | | | |
| 6. Guinea Pigs | | | | | |
| 7. Hamsters | | | | | |
| 8. Rabbits | | 669 | 136 | 23 | 828 |
| 9. Non-human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | | | |
| 12. Other Farm Animals | | | | | |
| | | | | | |
| 13. Other Animals | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual resea 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 app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in 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 )

| | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *( Type or Print )* | DATE SIGNED |
|---|---|---|
| | | 11/30/04 |

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

Foik

DEC - 8 2004

Column E Explanation

1. Registration Number: 93-R-0026
2. Number of animals used in these studies: 25
3. Species (common name) of animals used in the study: Dog, Rabbit
4. Explain the procedure producing pain and/or distress.

The 2 dogs assigned into Block E were used for a pharmacokinetics and toxicology dose range finding study. The procedures involved did not cause the category E classification; rather it was the systemic toxicity from the administration of the test articles that caused discomfort to the dogs in this category. The dogs had emesis and diarrhea on Day 1 (day of single iv dose administration), and again on Day 4. The female and male dog were euthanatized on Day 5 and 6 respectively. No analgesic or other drugs were given to the dogs since the use drugs may of have interfered with the uptake, distribution, or metabolism of the compound being tested, and ultimately interfere with the interpretation of the study results and the assessment of the test articles toxicity.

The 23 rabbits assigned to block E were used in (b)(4) pilot studies. The objective of the pilot was to understand the progression of (b)(4) so that possible therapies could be investigated. (b)(4) develops in humans with predisposing diseases (leukemia), those undergoing immunosuppressive therapy, and those with chronic lung disease (asthma, cystic fibrosis). The most common symptoms being (b)(4) In some chronic cases, little distress exists except for occasional bouts of hemoptysis (coughing up of blood). Under the right conditions, (b)(4) is rapidly fatal.

In establishing the (b)(4) model in rabbits, it was necessary to become familiar with the pattern that the disease takes and the associated clinical symptoms so distressed animals could be identified. Therefore, intervening with a therapeutic treatment would interfere with the study objectives of the infected untreated group. Additionally, the recognized treatment for (b)(4) was being given to a group of animals to establish the possible therapeutic dose. The most common clinical signs we saw in animals placed in column E were wheezing, labored breathing, general respiratory distress, diarrhea, and weight loss. When death was imminent the animals were humanely euthanatized.

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)

The purpose of the pharmacokinetics and toxicology dose range finding study was to determine the plasma elimination kinetics of the test compound and to evaluate toxicity after administration of a single iv dose in dogs. The minimum number of animals was used to conduct the range finding pilot study. The 2 dogs that developed abnormal clinical signs were euthanatized. Animal welfare concerns have been taken into consideration to ensure that the 2

dogs did not experience pain, discomfort or distress beyond what was necessary to obtain scientifically valid results.

The purpose of the (b)(4) study was to determine if the therapeutic drug, delivered in a novel way, could be given prophylactically. For comparison, an infected untreated control group was included in this study and these animals were placed in column E. Because we were familiar with the pattern that the disease takes and the associated clinical symptoms, we were able to anticipate which days the animals should start to show adverse clinical signs and so adequate staff was available to deal with animals in moribund condition and thus, alleviate undo distress in a timely manner through euthanasia. As previously mentioned, the disease progresses rapidly and an animal that appeared normal one day would develop respiratory distress the next day so therapeutic intervention would not be effective as a means to alleviate distress.

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: Food and Drug Administration (FDA) 21 CFR 321.23,a,5,ii,iii

   An Investigational New Drug (IND) submission requires: A summary of the pharmacological and toxicological effects of the drug in animals.

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

# ANNUAL REPORT OF RESEARCH FACILITY

*(TYPE OR PRINT)*

1. REGISTRATION NO. 93-R-0434 Customer NO 9193

Form Approved OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA include zip code)

UNIVERSITY OF CALIFORNIA, IRVINE
155 ADMINISTRATION BUILDING
IRVINE, CA 92697
(949) 824-5085

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

**FACILITY LOCATIONS(sites)**

See Attached Listing

**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 | | 38 | | | 38 |
| 5. Cats | | | 206 | | 206 |
| 6. Guinea Pigs | | 24 | | | 24 |
| 7. Hamsters | | 57 | 21 | | 78 |
| 8. Rabbits | 6 | 33 | 368 | 20 | 421 |
| 9. Non-Human Primates | | | | | |
| 10. Sheep | | | | | |
| 11. Pigs | | | 186 | | 186 |
| 12. Other Farm Animals | | | | | |
| Chicken | | 216 | | | 216 |
| 13. Other Animals | | | | | |
| Peromyscus | 136 | | 40 | | 40 |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate us of anesthetic, analgesic, and tranquilizing 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 regulation under the act, and it has requir3ed 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 us.

**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**

| SIG[illegible] FFICIAL | NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)* | DATE SIGNED |
|---|---|---|
| | | 11/19/03 |

**APHIS FORM 7023** (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete **PART 1 - HEADQUARTERS**

NOV 26 2003

UNIVERSITY OF CALIFORNIA, IRVINE

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

University Laboratory Animal Resources

147 BSA
Irvine, CA 92697-1310
Phone (949) 824-7298
FAX (949) 824-2003

**Animal Facilities at University of California, Irvine:**

Beckman Laser Institute
Bonney Research Laboratory (Center for Neurobiology of Memory and Learning)
Gillespie Neuroscience Research Facility
Hewitt Hall
Irvine Hall
McGaugh Hall
Medical Sciences I
Medical Surge II
North Campus Aviary
North Campus Air Pollution Health Effects Laboratory
Steinhaus Hall
UCIMC Building 55*
UCIMC Building 60*
University Research Park

* Located at the UCI Medical Center in Orange, California.

## Column E Explanation

1. USDA Registration number: 93-R-0434
2. Number of animals in Category E: 20
3. Species (common name): Rabbits
4. Procedure producing possible pain or distress.

The rabbit eye is inoculated with *Herpes simplex, type 1,* (herpetic eye disease). This animal model studies the processes regulating the latency and recrudescence of ocular herpes infections. Human patients with ocular herpes infections rarely report pain, but rather some patients report discomfort. It is thought that this infection is generally pain free because the viral infection damages nerve endings of the cornea resulting in loss of sensation. However, a small minority of infected rabbits (< 5%) show signs of irritation and may scratch at the skin around the orbit. In addition, <1 of infected rabbits may progress on to further complications such as encephalitis and seizures. Such rabbits are euthanized immediately.

5. Scientific justification why pain and/or distress could not be relieved, including methods or means used to determine that pain and/or distress relief would interfere with test results.

Treatment of the ocular infections was considered, and non-treatment was approved by the IACUC based on the following rationale.

- Although animals transiently develop clinical signs of disease (ie: conjunctivitis, iritis and keratitis, etc.), the condition does not appear painful to the majority of study subjects (see above). Assessment of pain and distress was performed by veterinary personnel.
- Topical drugs in the eye would interfere with the experimental infection and adversely affect the study results. Such treatment may actually enhance the infection rather than ameliorate it. In particular, , the ability to accurately measure the amount of virus (the major experimental outcome) in the eye at different time points after infection would be compromised by standard medical therapies.
- Review of laboratory records concerning this model. Over the preceding three years (performed at another institution), this laboratory used >1500 rabbits in similar research and <1% of the animals required euthanasia due to complications from the viral infection.
- Alternative searches using USDA approved databases were performed that validated the rabbit model and failed to identify alternative methodology or practices that would allow therapeutic intervention.

6. What, if any, federal regulations required this procedure?

Not applicable.