result in an order to cease and desist and to be subject to penalties as provided for in Section 2150. additional information. 0190-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

169

1. REGISTRATION NO. 22-R-0006 22R00060

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)
R.W. Johnson Pharmaceutical Resear
Route 202
P.O. Box 300
Raritan, NJ 08869-0602
Status: Active

NOV 29 1999

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

R.W. Johnson, PRI Raritan, NJ

R.W. Johnson, PRI Spring House, PA

R.W. Johnson, PRI LaJolla, CA

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		199*	291*	35	525
5. Cats					
6. Guinea Pigs		147*	461*	147	755
7. Hamsters					
8. Rabbits		686*	650*	168	1504
9. Non-human Primates		24*	116*	15*	155
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
Chinchillas	15				

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 OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL	DATE SIGNED
		11/19/99

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (OCT 88), which is obsolete.)

PART 1 - HEADQUARTERS

22R0006

Attachment 1

USDA ANNUAL REPORT (1998-1999)

NOV 29 1999

The following animals were reported on previous USDA reports under License #22R-006.

	Category B	Category C	Category D	Category E
Dogs	0	116	132	0
Guinea Pigs	0	37	55	0
Rabbits	0	54	153	0
Non-Human Primates	0	24	56	15

Animals Listed in Category E

During the reporting period, the R.W. Johnson Pharmaceutical Research Institute Institutional Animal Care and Use Committee (IACUC) approved the use of animals in Category E as follows:

SPECIES	NUMBER	PROCEDURE/JUSTIFICATION
Guinea Pigs	5	** Single dose IP Toxicology study
	78	Evaluation of aerosol anti-asthmatic agents – administration of anesthetics, analgesics or tranquilizing drugs will affect the procedure
	64	Involved in a behavioral test in which the pups were removed from the sow for a short period of time
Rabbits	138	** Oral and IV Toxicology study
	30	**Subcutaneous Toxicology study
Dogs	34	** Oral Toxicology study
	1	** Intravenous Toxicology study
Non-Human Primates	15	**Involved in a conflict test which, during the training phase, involves a mild electric stimulus to the tail

** Administration of anesthetics, analgesics or tranquilizing drugs must be withheld so as not to invalidate the evaluation of test compounds.

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NOV 24 2000

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.
21-R-0072, Cust Id 326

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*
Memorial Sloan-Kettering Cancer Ce
1275 York Avenue, Box 270
New York, NY 10021

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. 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	0	1	8	3	12
5. Cats	0				0
6. Guinea Pigs	0				0
7. Hamsters	0	4	19		23
8. Rabbits	0	162	18		180
9. Non-human Primates	0		7		7
10. Sheep	0				0
11. Pigs	0				0
12. Other Farm Animals	0				0
13. Other Animals	0				0

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 [illegible]43).

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
		11/17/00

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

PART 1 – HEADQUARTERS

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NOV 2 4 2000

FACILITY SITES LISTING

Licensee/Registrant Name: Memorial Sloan-Kettering Cancer Center

License/Registration Number: 21-R-0072

Please list below all sites that house regulated animals under the above number. Be sure to include all requested information. If the line does not apply, please mark it N/A. If you have more than three (3) sites copy this form as many times as needed before filling in the sites.

Site No. 1 Name/Department: Research Animal Resource Center

Address: 4325East 68th Street

New York, NY 10021

Building: Kettering Laboratory Building

Floor/Room: Basement, 3, 10 11 Floors

Contact Person: Phone No.

Site No. 2 Name/Department: Weill Medical College of Cornell University

Address: 1300 York Avenue

New York, NY 10021

Building: Harkness Building

Floor/Room: 7th Floor

Contact Person: Phone No.

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.

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1. Registration Number: 21-R-0072

2. Number 3 of animals used in this study.

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

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

Dogs were administered desoxyepothiloneB (dEpoB), a novel anti-cancer drug, at toxic doses, in preparation for human clinical trials. One dog received a vehicle control, one dog received a sub-toxic dose, and one each received low, medium and high toxic doses. The compound was administered as a single iv injection or a slow iv infusion. Preliminary studies in mice revealed potential toxic effects of dEpoB were weight loss and mild leukopenia. Studies in dogs were required because the half-life of dEpoB is similar in human and dog serum; the half-life of dEpoB in mouse serum is much shorter than humans and would not adequately reveal the human toxicity profile.

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).

As is standard practice for toxicity studies at MSKCC, dogs receiving toxic doses of drugs are placed in category E prospectively. All animals exhibiting mild signs of toxicity are provided supportive fluid and antibiotic therapy. Animals exhibiting signs of moderate to severe distress are euthanized. Analgesics were not administered because they could interfere with the toxic effect of the test compound thereby invalidating the findings. Furthermore, the type of pain and distress induced by the expected toxicity would not necessarily be relieved by the use of analgesics, and therefore supportive therapy and euthanasia was determined to be the appropriate method for relieving moderate to severe pain and distress resulting from drug-induced toxicity. These determinations were based on the investigator's experience with the novel compound, literature searches conducted on 6/8/99, and IACUC deliberations.

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_____

Revised 11/27/00

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. 47-R-0010 CUSTOMER NO. 1550

FORM APPROVED OMB NO. 0579-0036

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
(402) 289-6300

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	0	298	48	7	353
5. Cats	0	352	41	0	393
6. Guinea Pigs	0	366	0	199	565
7. Hamsters	255	2496	0	1262	3758
8. Rabbits		6	482	0	488
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	9	221	5	92	318

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)

ove is true, correct, and complete (7 U.S.C. Section 2143)

SIGNAT

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

DATE SIGNED 11/25/03

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PART 1 - HEADQUARTERS

FEB 27 2004

All redactions on this page are pursuant to (b)(4).

Registration No. 47-R-0010

2003 USDA ANNUAL REPORT OF RESEARCH FACILITY

REGISTRATION No. 47-R-0010

Column "E" Entries

I. Dogs:

A total of seven dogs are listed in Column E. Four dogs became ill as part of a viral challenge as mandated by [redacted] and European Pharmacopoeia Monograph 01/2002:0964. Pain and distress-relieving drugs were not utilized in these tests since they would mask the effects of the virulent challenge. Three dogs became ill following bacterial challenge. The treatment of the dogs was delayed in order to evaluate clinical signs for development of a new bacterin as per VS Memorandum 800.202. IACUC has approved all of these studies.

II. Guinea Pigs:

A total of 199 guinea pigs are listed in Column E. The guinea pigs were used in 11 [redacted] In each potency test, one or more serials were tested concurrently in order to reduce the number of animals by sharing the control-unvaccinated group. A total of 18 serials were tested. One hundred forty-four (144) animals were used as vaccinated and fifty-five (55) animals as unvaccinated controls. The vaccine potency test was performed according to USDA-mandated methods specified in [redacted] which requires death as an endpoint. The 55 control animals died or were euthanized as a result of the bacterial challenge. While all 144 vaccinated animals were protected from death, the nature of the challenge material induced irritation at the injection site for the duration of the three-day potency test. Injection site irritation is expected for this type of challenge.

This test is required by regulation as a proof of [redacted] potency to be conducted on each serial of vaccine produced. Death of guinea pigs in this test has been used for many years to indicate lack of protection from [redacted] Clostridial disease in guinea pigs almost always results in acute onset and rapid death. The rapid progression of the disease in the guinea pig gives little opportunity for intervention. Furthermore, pathology would likely be impacted by use of anti-inflammatories. For this reason, neither our company, 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 private communication with USDA-CVB-LPD) 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* test alternatives for products that require this test and our company has actually developed a test that is being considered for use. Until a validated USDA-CVB approved alternative is available, the standard test is obligatory. No alternative exists at this time, and no CVB-approved means of relieving pain and distress for this use of guinea pigs are yet available.

III. Hamsters:

A total of 1262 hamsters are listed in Column E. The hamsters were used for [redacted] potency testing. Tests were conducted according to USDA-mandated methods specified in [redacted] These tests are required by regulation as 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 from 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 our company 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 private communication with USDA-CVB-LPD) 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 alternative for products that require this test and our company has actively participated in this effort. Until 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.

IV. Mink:

A total of 92 mink are listed in Column E. The mink were used in potency tests for a [redacted] vaccine. Tests were conducted according to USDA-mandated methods specified in [redacted]

The viral enteritis potency test is required by regulation as a proof of viral enteritis vaccine potency to be conducted on each serial of vaccine products. The challenge with virulent virus induces clinical diarrhea that can lead to death. In cases that this happens, the rapid progression of the disease in the mink gives little opportunity for intervention.

The Clostridial potency test is required by regulation as a proof of Clostridial vaccine potency to be conducted on each serial of vaccine produced. Death of mink in this test has been used for many years to indicate lack of protection from Clostridial disease. Clostridial toxin challenge of mink almost always results in acute onset and rapid death. The rapid progression of the disease in the hamster gives little opportunity for intervention.

For both of these required potency tests, pathology would likely be impacted by the use of anti-imflammatories. For this reason, neither our company 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 private communication with USDA-CVB-LPD) 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 animal testing for product release. Our company has been an active industry partner in these efforts. Until validated USDA-CVB approved alternatives are available, the standard tests are 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.

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-0065 CUSTOMER NO. 1476

FORM APPROVED OMB NO. 0579-0036

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

UNIVERSITY OF TEXAS
1515 HOLCOMBE BLVD
HOUSTON, TX 77030
(713) 792-2780

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		40		40
5. Cats					
6. Guinea Pigs					
7. Hamsters	0	247	13		260
8. Rabbits	17	52	186		238
9. Non-Human Primates	452	468	47		515
10. Sheep	82	31	56	1	88
11. Pigs	23	17	45		62
12. Other Farm Animals					
Cattle		1			1
13. Other Animals					
Horses		1			1
Geese		8			8

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
		11/3/03

which

HEADQUARTERS

NOV 14 2003

APHIS Form 7023 Site List

The following sites have been reported by the facility.

Registration Number:	74-R-0065
Customer Number:	1476
Facility:	UNIVERSITY OF TEXAS 1515 HOLCOMBE BLVD HOUSTON, TX 77030 (713) 792-2780

MD ANDERSON CANCER CTR
1515 HOLCOMBE
HOUSTON, TX 77030

DEPT OF VETERINARY SCIENCES
650 COOL WATER DRIVE
BASTROP, TX 78602

UT MD ANDERSON CANCER CENTER
PARK ROAD 1C
SMITHVILLE, TX 78957

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-0065

2. Number 1 of animals used in this study.

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

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

ACUF # 07-98-04922

A surgical procedure is used to ligate a superficial motor nerve of the foreleg. If neuropathic pain develops, the animal is maintained on drugs to relieve the neuropathic pain except during a brief period between experiments to evaluate alternative neuropathic pain relief drugs. Animals which develop neuropathic pain are maintained 63-70 days, during which time there are 3 episodes of analgesic evaluations. The animal is then euthanized.

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 model is designed to evaluate new methods of treating human neuropathic pain, by the assessment and evaluation of analgesics delivered via spinal infusion.

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):

None
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 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. 93-R-0026 | CUSTOMER NO. 1182 | FORM APPROVED OMB NO. 0579-0036

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

SRI INTERNATIONAL
333 RAVENSWOOD AVENUE
MENLO PARK, CA 94025
(650) 859-2000

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		86	12	0	98
5. Cats					
6. Guinea Pigs				5	5
7. Hamsters					
8. Rabbits	26*	202	~~43~~ 28*	~~14~~ 0*	~~230*~~ 256
9. Non-Human Primates		* Changes per Itr From facil. dated 6/22/04 mk			
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 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)

ATE SIGNED 11/21/03

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

PART 1 - HEADQUARTERS

Received FAX 11/21/03

All redactions on this page are pursuant to (b)(4).

Column E Explanation

1. Registration number: 93-R-0026

2. Number of animals used in these studies: 16

3. Species (common name) of animals used in these studies: Rabbit, Guinea Pig

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

   Five (5) guinea pigs were euthanized via decapitation without anesthetic.

   Eleven (11) rabbits experienced Category E pain/distress for approximately 1-2 days each from dose administration of [redacted] into the lungs. The [redacted] created infection of the lungs. When it was determined that the rabbits were experiencing pain and/or distress, the rabbits were euthanized.

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 5 guinea pigs were used as a tissue source for ileal smooth muscle bioassays. The ileum is very sensitive to anesthetics. When anesthetic is used the tissues don't contract and they are insensitive to the opiates that were being tested. For this reason, administration of anesthesia prior to decapitation was contraindicated.

   Each of the 11 rabbits was on a continuous regimen of antibiotics to treat the underlying cause of this pain &/or discomfort. Also, when personnel identified this condition, the rabbit was euthanized as soon as possible.

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 312.23,a,5,ii,iii

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

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.: 072

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 16-R-0029
CUSTOMER NUMBER: 55

FORM APPROVED
OMB NO. 0579-0036

Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

NOV 2 3 2004

Telephone: (203) -798-9988

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)

175 Briar Ridge Road
Ridgefield, CT 06877

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 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 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	42	16	24	8	48
5. Cats					
6. Guinea Pigs			75		75
7. Hamsters					
8. Rabbits				10	10
9. Non-human Primates	164		8	216	224
10. Sheep					
11. Pigs			4		4
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)

SIGNATURE OF

DATE SIGNED 11/01/04

APHIS FORM 7023
(AUG 91) (... is obsolete.)

The 8 dogs assigned to column E of this report were included in toxicology or safety assessment procedures in which, to meet Food and Drug Administration requirements under Good Laboratory Practice regulations (21 CFR 58.120, 43 CFR 60013) a limited number of animals must be exposed to test compound dose levels toxic to the animal. Clinical signs produced by some test compounds at toxic dose levels may be distressful or painful to the animal, if only transiently. To intercede prematurely would invalidate the procedure, requiring its repetition and the consequent use of more animals.

The 10 rabbits assigned to column E of this report were used for hyperimmunization procedures (polyclonal antibody production) in which adjuvant associated with the antigen of interest produced localized discomfort typical of a subacute inflammatory reaction. The lesions were treated topically to minimize discomfort, and in all cases the minimum quantity of least irritating adjuvant was employed that would not have necessitated the use of additional animals. The protocol permits 10-20 intradermal injection sites which may be pruritic or transiently painful when subjected to normal postural adjustments. The use of systemic analgesics during the several week duration of the process is regarded as inappropriate, since these agents interfere with the antibody production process (e.g., corticosteroids), or have systemic side effects in chronic dosage (appetite suppression, constipation). Although the injection sites are monitored daily for signs of excessive inflammation and treated locally with emollients, local anesthetics and antibiotics as indicated, a conservative classification acknowledges the potential for distress associated with what is an iatrogenic dermatitis.

Primates assigned to column E of this report were used in various toxicology/safety assessment procedures, pharmacologic studies of the inflammatory response or evaluation of the immunomodulatory effects of test compounds.

39 cynomolgus macaques were injected parenterally with compounds intended to produce [redacted] Although doses are titrated to produce the minimum physiologic change compatible with the appropriate evaluation of the test anti-inflammatory compound, normal physiologic variation among animals, the side effects of up to four hour sedation throughout the test period and repeated use of the same animals to test a succession of compounds produces transient anorexia and limited signs of depression during the 24-hour post-test period. We feel this could be distressful to the animal and have conservatively assessed the procedure accordingly.

22 squirrel monkeys are used as a model of cell mediated immunity (CMI) in which they are sensitized by antigen in an adjuvant vehicle appropriate to the route, dosed with test compound by a variety of routes and then skin tested with the original antigen. Although antigen dose is minimized, systemic reactions include inappetence and depression; local reactions at injection sites are those associated with minimal acute inflammation. Discomfort is attenuated through the use of analgesic drugs but, because an inflammatory condition is induced and clinical signs may appear, it is anticipated that the monkeys may potentially experience the discomfort which human beings feel during the analogous condition.

155 rhesus macaques were included in toxicology or safety assessment procedures in which, to meet Food and Drug Administration requirements under Good Laboratory Practice regulations (21 CFR 58.120, 43 CFR 60013) a limited number of animals must be exposed to test compound at dose levels toxic to the animal. Clinical signs produced by some test compounds at toxic levels may be distressful or painful to the animal, if only transiently. To intercede prematurely would invalidate the procedure under the cited regulations, requiring repetition of the study and the consequent use of more 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 21! NOV 24 2004 See attached form for additional information. Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

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

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

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

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			46		46
5. Cats			1		1
6. Guinea Pigs		381			381
7. Hamsters			76		76
8. Rabbits			65		65
9. Non-human Primates			12	6	18
10. Sheep			5		5
11. Pigs			94		94
12. Other Farm Animals					0
13. Other Animals					0

WMC houses 7 non-human primates and 4 rabbits belonging to MSKCC (Reg. # 21-R-0072). These animals are counted on MSKCC's annual report and not included on this report.

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
X		11/22/04

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

APHIS form 7023 Site List
Registration #: 21-R-0114
Customer Number: 336
Facility: Weill Medical College
1300 York Avenue
New York, NY 10021
(212) 746-1077

Harkness and S Building
1300 York Avenue
New York, NY 10021
County: New York

Kips Bay Building
East 69th Street
New York, NY 10021
County: New York

Citigroup Imaging Center
515 East 72nd Street
New York, NY 10021
County: New York

Kettering Lab
425 East 68th Street
New York, NY 10021
County: New York

Burke Medical Research Institute
785 Mammaroneck Avenue
White Plains, NY 10605
County: Westchester

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

1. Restriction of water in non-human primates (for behavioral training) = 3 Protocols

2. Pair housing two (2) "Group 3" non-human primates in a cage with floor space of 8.08 sq. ft. instead of the required 8.6 sq. ft.

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 a 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.
   Rhesus macaque

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 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

FEB 2) 2005

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.: 0

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

October 1, 2003 to September 30, 2004

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

AMENDED

1. **CERTIFICATE NUMBER:** 21-R-0199
CUSTOMER NUMBER: 537

FORM APPROVED
OMB NO. 0579-0036

Roswell Park Cancer Institute
Roswell Park Cancer Institute Corp
Buffalo, NY 14263

Telephone: (716) -845-2300

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)

Medical Research Complex
Cancer Cell Center

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 proceduras, 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		4	71	4	79
5. Cats					
6. Guinea Pigs					
7. Hamsters					
8. Rabbits		2	13		15
9. Non-human Primates					
10. Sheep					
11. Pigs			3		3
12. Other Farm Animals					
13. Other Animals					
Wild mice	404	926			926

ASSURANCE STATEMENTS

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

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

Column E Explanation

FEB 2 3 2003

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-0032

2. Number C=4 D=71 E=4 of animals used in this study.

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

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

ALL OF OUR ANIMALS ARE USED FOR PRECLINICAL TOXICOLOGY TESTING. PAIN OR DISTRESS IS CAUSED BY ADMINISTRATION OF CYTOTOXIC DRUGS THAT CAUSE A VARIETY OF TOXICITIES, SUCH AS MYELOSUPRESSION, GASTROINTESTINAL TOXICITY, ANOREXIA, ETC.

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 POINT OF PRECLINCIAL TOXICOLOGY TESTING IS TO DETERMINE A SAFE STARTING DOSE IN MAN, TO DETERMINE THE FULL CONSTELLATION OF TOXICITIES BOTH IMMEDIATE (WITH HOURS OR DAYS) AND DELAYED (WEEKS TO MONTHS) THAT MAY OCCUR, AND TO EXCLUDE DRUGS FROM HUMAN TESTING THAT SHOW A PATTERN OF UNACCEPTABLE TOXICITY (HEART FAILURE, BLINDNESS, ETC.). WHILE THE TOXICITIES THAT OCCUR THAT MAY CAUSE DISTRESS ARE OFTEN TREATABLE, THAT WOULD BE COUNTER TO THE GOALS OF TESTING, WHERE INFORMATION REGARDING THE FREQUENCY, MAGNITUDE AND REVERSIBILTY OF TOXICITIES ARE ALL IMPORTA TO UNDERSTAND AND STUDY.

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 2149. NOV 1 9 2004 See attached form for additional information. Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 22-R-0009
CUSTOMER NUMBER: 519

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Novartis Pharmaceuticals Corporation
Bldg 437/1329
One Health Plaza
East Hanover, NJ 07936

Telephone: (973)-781-007

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 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 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	-	336	14	27	377
5. Cats	N/A	-	-	-	-
6. Guinea Pigs	-	42	-	-	42
7. Hamsters	N/A	-	-	-	
8. Rabbits	1	398	-	67	466
9. Non-human Primates	133	382	102	35	652
10. Sheep	N/A	-	-	-	-
11. Pigs	N/A	-	-	-	-
12. Other Farm Animals	N/A	-	-	-	-
13. Other Animals	N/A	-	-	-	-

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 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 CHIEF EXECUTIVE OR INSTITUTIONAL OFFICIAL	NAME OF CHIEF EXECUTIVE OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
		10-17-04

APHIS FORM 7023 (Replaces VS Form 7023, which is obsolete.)
(AUG 91)

USDA ANNUAL REPORT OF RESEARCH FACILITY FOR 2003-2004
NOVARTIS PHARMACEUTICALS CORPORATION
USDA Registration No. 22-R-0009

Summary of the NACUC approved exceptions to the Standards and Regulations:
Canine Exercise Exemptions

	Protocol Title	Species	Number	Days Without Exercise	Reason
1.	Absorption, Metabolism, and Excretion After A Single Oral or IV Dose in the Dog	Dog	6	9	Quantitative collection of excreta, containment of radioactivity
2..	Telemetry Device Implantation and Holding Monkeys intended for Use on Safety Pharmacology Studies	Dog	1	10	Treatment of Interdigital pyoderma
3.	Telemetry Device Implantation and Holding Monkeys intended for Use on Safety Pharmacology Studies	Dog	1	22	Treatment for Lameness

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 32 . Number of animals classified as category "E" - 3 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Three animals on this study experienced clinical conditions that required unscheduled euthanasia. These three animals had clinical issues that required them to be sacrificed early. The problems included a recurring salivary cyst, a fracture injury of the pelvis and a severe dermatitis.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 24 . Number of animals classified as category "E" - 1 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects resulting in diarrhea of greater than 5 days duration.

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 overall clinical condition noted was not deemed so severe that the animal could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 4 . Number of animals classified as category "E" - 2 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Two animals on this study experienced compound related effects of being found in a moribund state and were therefore euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 24 . Number of animals classified as category "E" - 2 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Two animals on this study experienced compound related effects resulting in decreased locomotor activity, recumbency and labored breathing that lead to a moribund state.

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)

   These two animals were humanely euthanized as soon as the clinical signs noted above were observed.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 10 . Number of animals classified as category "E" - 2 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Two animals on this study experienced compound related effects of being found in an moribund states and were therefore euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 32 . Number of animals classified as category "E" - 12 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Twelve animals on this study experienced compound related effects of being found in a moribund state and were therefore euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 31 . Number of animals classified as category "E" - 1 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects of severe labored breathing and lethargy and was therefore euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 24 . Number of animals classified as category "E" - 1 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects resulting in diarrhea for more than 5 consecutive days while on study.

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 overall clinical condition observed was not deemed so severe that the animal could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM

Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 24 . Number of animals classified as category "E" - 2 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Two animals on this study experienced compound related effects resulting in diarrhea for more than 5 consecutive days while on study.

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 overall clinical condition observed was not deemed so severe that the animal could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 44 . Number of animals classified as category "E" - 1 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects resulting in diarrhea of greater than 5 days duration.

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 overall clinical condition noted was not deemed so severe that the animal could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM

Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 15 . Number of animals classified as category "E" - 15 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Nine rabbits animals on this study experienced compound related effects and were euthanized. Six animals were found dead while on study.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 30 . Number of animals classified as category "E" - 4 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Three animals on this study experienced compound related effects and were euthanized. One other rabbit was found dead while on study.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM

Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 100 . Number of animals classified as category "E" - 5 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Three animals on this study experienced compound related effects and were euthanized. One of these three was found to be moribund and the other two had abortions. Two additional animals were found dead while on study.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

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OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 30 . Number of animals classified as category "E" - 6 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Three rabbits on this study experienced compound related effects and were euthanized after they were found to have had abortions. The other three were euthanized after they were found to have had premature deliveries.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM

Study Number (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 30 . Number of animals classified as category "E" - 5 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   One rabbit on this study experienced compound related effects resulting in the animal being found in a moribund state. This animal was euthanized. Four rabbits were found dead while on study.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 22 . Number of animals classified as category "E" - 18 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Four rabbits on this study experienced compound related effects and were euthanized. Fourteen rabbits were found dead while on study.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 100 . Number of animals classified as category "E" - 14 .

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

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

   These rabbits were dosed with a pharmaceutical compound.

   Fourteen rabbits on this study experienced compound related effects and were euthanized.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 14 . Number of animals classified as category "E" - 1 .

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

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

   These marmosets were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects that included diarrhea for five days duration.

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 overall clinical condition noted was not deemed so severe that the animal could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 8 . Number of animals classified as category "E" - 1 .

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

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

   These marmosets were dosed with a pharmaceutical compound.

   One animal on this study experienced compound related effects that resulted in this animal being found in a moribund state.

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)

   This animal was immediately scheduled for humane euthanasia and necropsy but it died in transit.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 24 . Number of animals classified as category "E" - 2 .

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

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

   These marmosets were dosed with a pharmaceutical compound.

   Two of the animals on this study experienced compound related effects. One animal had diarrhea for greater than 5 days duration and the other was sacrificed unscheduled because of multiple clinical signs such as weight loss, decreased locomotor activity, emesis and anorexia.

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 overall clinical conditions observed in one of the two animals on this study was not deemed so severe that the animal could not continue on the study. Relieving the cause of the diarrhea would have defeated the purpose of the study. As soon as there were signs indicating that the other animal was experiencing pain and distress, it was humanely euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 72 . Number of animals classified as category "E" - 8 .

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

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

   These marmosets were dosed with a pharmaceutical compound.

   Seven of the animals on this study experienced compound related effects such as hypothermic, lethargy, anorexia and diarrhea that resulted in this animal being euthanized. One other animal on this study was found dead.

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)

   Except for the one animal that was found dead, these animals were immediately scheduled for humane euthanasia and necropsy as soon as signs of pain/distress were observed.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 40 . Number of animals classified as category "E" - 6 .

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

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

   These marmosets were dosed with a pharmaceutical compound.

   Six of the animals on this study experienced compound related effects such as diarrhea for greater than 5 days duration.

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 overall clinical conditions observed was not deemed so severe that the animal could not continue on the study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

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OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 12 . Number of animals classified as category "E" - 2 .

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

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

   These monkeys were dosed with a pharmaceutical compound.

   Two animals on this study experienced compound related effects that resulted in these animals being found in a moribund states therefore they were euthanized unscheduled.

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)

   As soon as there were signs indicated that an animals was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

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OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 32 . Number of animals classified as category "E" - 7 .

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

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

   These monkeys were dosed with a pharmaceutical compound.

   Seven animals on this study experienced compound related effects such as emesis, decreased locomotor activity, ataxia, hunched posture and piloerection leading to a moribund states and were therefore euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

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OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 32 . Number of animals classified as category "E" - 5 .

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

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

   These monkeys were dosed with a pharmaceutical compound.

   Five animals on this study experienced compound related effects resulting in diarrhea for more than five consecutive days in duration.

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 overall clinical condition observed was not deemed so severe that the animals could not continue on study. Relieving the cause of the diarrhea would have defeated the purpose of the study.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

OPTIONAL COLUMN E EXPLANATION FORM
Study Number: (b)(4) [redacted]

1. Registration Number: 22-R-0009

2. Number of animals used in this study: 10 . Number of animals classified as category "E" - 3 .

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

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

   These dogs were dosed with a pharmaceutical compound.

   Three animals on this study experienced compound related effects that resulted in poor food consumption and severe body weight loss therefore these animals were euthanized unscheduled.

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)

   As soon as there were signs indicating that an animal was experiencing pain or distress, it was euthanized.

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):

   The general reference is 21 CFR 312.23(a)(8). This reference indicates that there are guidelines available from the FDA that describe ways in which these requirements may be met. More specific guidelines may be found in the following:

   1) M3 Nonclinical safety studies for the conduct of human clinical trials for pharmaceuticals published in the Federal Register on November 25, 1997 (62 FR 62922)

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 2 4 2004

See attached form for additional information.

Interagency Report Control No. 7

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 22-R-0036
CUSTOMER NUMBER: 181

FORM APPROVED
OMB NO. 0579-0036

Schering Corporation
Schering-Plough Research Inst.
2015 Galloping Hill Road
Kenilworth, NJ 07033

Telephone: (908) -298-4000

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 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 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 reas such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	44	135	132	4	271
5. Cats	0	0	25	0	25
6. Guinea Pigs	0	4741	968	0	5709
7. Hamsters	0	0	186	0	186
8. Rabbits	2	314	83	7	404
9. Non-human Primates	142	364	407	8	779
10. Sheep	0	0	0	0	0
11. Pigs	0	0	6	0	6
12. Other Farm Animals	0	0	0	0	0
13. Other Animals					
Gerbils	0	168	2320	0	2488

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 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)

SIG

DATE SIGNED 12-21-04

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

42

NOV 2 4 2004

Registration Number: 22-R-0036

November 19, 2004

Elizabeth Goldentyer, DVM
UNITED STATES DEPARTMENT OF AGRICULTURE
Animal and Plan Health Inspection Service
Regulatory Enforcement and Animal Care
Eastern Region Office
920 Main Campus Drive
Suite 200
Raleigh, NC 27606

Dear Dr. Goldentyer:

Listed below are comments to accompany the annual report of research facilities for site number 1.

A. Summary of exceptions to the regulations and standards:

The environmental enrichment program has exceptions for social housing for nonhuman primates. Twenty-one rhesus monkeys are housed separately due to special study requirements for controlling and monitoring food consumption as part of the research projects. Thirteen cynomolgus monkeys were housed separately for brief periods (1-5 days) while participating in telemetric monitoring studies and six cynomolgus monkeys were housed separately for 14 days for individual collection of excreta in a radioisotope labeled compound metabolism study. All the animals are included in all the other aspects of the environmental enrichment program. The protocols with an exemption are approved by the IACUC and reviewed during the semi-annual program review.

One exception to the canine exercise program is to be reported. It involved the use of special canine metabolism cages for radioisotope labeled drug metabolism studies to safely and accurately collect excreta. The canine metabolism cages provide greater than 100% require floor space, but less than 200% of required space for exercise. The period of time in the cages vary with the test compound and study. This study lasted for 37 days. Positive human interaction is greatly increased during this period. Five canines were involved with these studies. The protocol with the exemption is approved by the IACUC and reviewed during the semi-annual program review.

B. General Column "E" Justification Statement:

Six cynomolgus monkeys developed unexpected acute complications during a study. The animals were closely monitored by the research and veterinary staff during the study. When significant complications developed, the animals were humanely euthanized without delay. Due to their illness, they are retrospectively being reported in column E.

Registration number 22-R-0036

Listed below are comments to accompany the annual report of research facilities for site number 2.

A. Summary of exceptions to the regulations and standards:

There were some exceptions to the pair housing requirement of our IACUC approved program for the psychological well-being of non-human primates. Most exemptions were for approximately two weeks in duration. Three hundred forty-four non-human primates were single-housed for two out of the five week quarantine period for the purposes of acclimation and health assessment; nineteen for various periods of time while suitable cage mates were tried; and ten because they lacked suitable cage mates.

B. General Column "E" Justification Statement:

Listed below are the animals that retrospectively or prospectively experienced or may have experienced pain or distress while on study.

One non-human primate became ill on study and was given symptomatic treatment. The animal was euthanized due to a lack of response to the treatment and weight loss. One primate on study developed a toe injury unrelated to the study and injury was treated by the veterinary staff. The injury did impair some of the non-human primate's mobility but remained on study. All studies are approved by the IACUC and conducted in accordance with the FDA requirements [FDA 21 CFR 312.23 (a) (8), 21CFR 58, 62 FR62922 and 59 FR 48746].

One canine had a very acute and unexpected death while on study. Three canines experienced some short seizures while on study. On of the studies objectives was to monitor for seizures and treatment would have interfered with compounds safety evaluation. The animals were closely monitored by the veterinary and research staff. All studies are approved by the IACUC and conducted in accordance with the FDA requirements [FDA 21 CFR 312.23 (a) (8), 21CFR 58, 62 FR62922 and 59 FR 48746].

Six rabbits developed unexpected terminal medical complications while participating in a study. Of the six rabbits, 4 died suddenly and 2 were humanely euthanized. One other rabbit experienced abnormal posture and tremors but was well enough to complete the study. All studies are approved by the IACUC and conducted in accordance with the FDA requirements [FDA 21 CFR 312.23 (a) (8), 21CFR 58, 62 FR62922 and 59 FR 48746].

Registration Number: 22-R-0036

ID:181

Site 1
Schering Corporation
Schering-Plough Research Institute
2000 Galloping Hill Road
Kenilworth, NJ 07033
(908) 298-4000

Site 2
Schering Corporation
Schering-Plough Research Institute
P.O. Box 32 Route 94
Lafayette, NJ 07848
(973) 940-4100

"A" E. Slauter
S. Bellen

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-AR

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 42-R-0001 | CUSTOMER NO. 1573 | FORM APPROVED OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
ANUL REPRLPOTNF

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

DIAMOND ANIMAL HEALTH INC
2538 SE 43RD STREET
DES MOINES, IA 50327

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)

DIAMOND ANIMAL HEALTH
DES MOINES, IA 50327

DIAMOND ANIMAL HEALTH
CARLISLE, IA 50047

COPY FOR YOUR INFORMATION

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			22		22
6. Guinea Pigs		164	262		426
7. Hamsters		2689		2606	5295
8. Rabbits			355		355
9. Non-Human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
Cattle	15	213			213
13. Other Animals					

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. (Print)	DATE SIGNED
		11/05/2004

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 0150-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 42-R-0001 CUSTOMER NO. 1573

FORM APPROVED OMB NO. 0579-0036

CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY ANUL REPRLPOTNF

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, Include ZipCode)*

DIAMOND ANIMAL HEALTH INC
2538 SE 43RD STREET
DES MOINES, IA 50327

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

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
Horses		4			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)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
		11/05/2004

APHIS FORM 7023A (AUG 91)

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

PART 1 - HEADQUARTERS

1. Registration Number: 42-R-0001 / 1573

2/3. Species (common name) & Number of animals used in this study:

Hamsters (2606)

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

To satisfy Federally mandated testing for Leptospira bacterins a vaccination-challenge model is used to determine potency of the vaccine. Virulent Leptospira organisms are injected intraperitoneally into hamsters to determine the potency of the bacterin and LD50 of the Leptospira suspension. Leptospira causes death in unprotected (unvaccinated) hamsters. From the comparison of the protected (vaccinated) live hamsters to the unprotected dead hamsters, the potency of the bacterin and the LD50 are obtained.

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)

Interventions, such as analgesics and antibiotics, would likely prolong the course of the disease, and may prevent or delay death, thus interfering with the test results. Death is the endpoint requirement for this potency test. Our firm has been working with the CVB regarding early endpoints under 9 CFR 117.4 and USDA, APHIS Center for Biologics (CVB) Notice No. 04-09. Please see the timeline as follows, 12-16-03 We received a letter from Dr. Koch asking us to explain the hamsters in Category E. 1-9-04 I called Dr. Koch to discuss early endpoints. She suggested I contact our CVB reviewer assigned to this firm. 1-14-04 I contacted our CVB reviewer and she stated in an email, "...the information that I currently have is that early endpoint has not been authorized in Outlines of Production" 1-15-04 I wrote to Dr. Koch indicating CVB's position 2-6-04 Dr. Koch called and said CVB told her they would allow an Outline change. 2-17-04 I emailed our CVB reviewer with this information and she checked with her supervisors and said they hadn't heard anything differently from the January decision. Attached to my email was a draft protocol, "Data Collection for Humane Endpoint Study," for her to look at. 3-10-04 I called Dr. Koch and left word for her to return my call to discuss. 3-23-04 Dr. Koch called me and said she had talked to Dr. Rick Hill (CVB Director). He stated that the CVB was coming out with guidelines about obtaining approval for early endpoints. 4-5 through 4-7-04 Attended "Technology and Approaches to Reduce, Refine and Replace Animal Testing" sponsored by APHIS in Ames, IA. 4-7 through 4-9 Attended "APHIS Veterinary Biologics Public Meeting" in Ames. This meeting also had information regarding early endpoints. 4-12-04 CVB reviewer faxed to me CVB Notice No. 04-09 "Use of Humane Endpoints in Animal Testing of Biological Products." 4-27-04 Dr. Belin, our AW inspector, sent the CVB Notice to me. 7-26-04 I called our reviewer to discuss the protocol, notice, and what our firm's statistician's thoughts were on numbers of hamsters needed to generate data. 7-28-04 Our reviewer emailed regarding data we needed to submit to support an Outline change. 8-27-04 I sent our reviewer another draft of a protocol with data capture forms. She replied that the "...list looked good for collecting data." 9-2-04 Final version of protocol reviewed and signed. Sept. '04 conducted pilot study. Concluded needed better method of identifying individual hamsters. 10-13-04 Meeting with Animal Care staff to discuss next study, id'ing hamsters, and revising forms. 10-26-04 Started a second pilot study. When we have accumulated sufficient data it will be submitted to CVB. We will ask for an Outline Change based on the data and the 9 CFR 117.4. CVB will review the data and hopefully allow the Outline change so that we can euthanize the hamsters "...exhibiting clinical signs consistent with the expected disease pathogenesis..." per CVB Notice no. 04-09. I would be glad to provide copies of any of the above correspondence.

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 113.101, 113.102, 113.103, and 113.104. CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

suit in an order to cease and desist and to be subject to penalties as provided for in Section 21

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 42-R-0009
CUSTOMER NUMBER: 1578

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

COPY FOR YOUR INFORMATION

Fort Dodge Laboratories
Division Of Wyeth
800 5th St Nw
Fort Dodge, IA 50501

Telephone: (515) -955-4600

04/05/05

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)

800 5th Street NW, Fort Dodge, IA 50501 FACILITY LOCATIONS (Sites) - See Attached Listing 2973 Highway 18 East, Charles City, IA 50616

2000 Rockford Road, 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 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	203	1029	73	268	1370
5. Cats	0	1161	7	128	1296
6. Guinea Pigs	0	4874	61	0	4935
7. Hamsters	0	12,784	0	8171	20,955
8. Rabbits	0	454	1408	0	1862
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	6	0	0	6
12. Other Farm Animals Cattle	0	8	0	0	8
Horses	0	14	0	0	14
13. Other Animals Goats	0	8	0	0	8
Gerbils	0	10	0	0	10
Ferrets	0	8	0	0	8

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 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)

SIGNA

DATE SIGNED
NOV 16,04

APHIS FORM 7023
(AUG 91)

h is obsolete.)

NOV 24 2004

COPY FOR YOUR INFORMATION

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

1. **Species: Canine**

2. **Number of animals achieving Cat. E in this study: 119**

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

   The dogs were inoculated subcutaneously with (b)(4) the organism that causes the disease canine (b)(4) They were then observed for clinical signs of (b)(4) to evaluate the ability of experimental vaccine to protect against the disease.

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

   The studies were required to evaluate a new vaccine's ability to protect against canine (b)(4) 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. Currently no alternatives to the use of dogs exist for this procedure. Challenge with (b)(4) may cause severe disease, which will result in a certain degree of pain and distress. Since the interpretation of the results depends on the clinical signs of the disease, treatment with antipyretic, corticosteroids, and antibiotics for pain and distress would alter the results.

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

   (b)(4)

   (b)(4)

   (b)(4)

NOV 24 2004

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

1. **Species: Canine**

2. **Number of animals achieving Cat. E in this study: 80**

3. **Explanation of the procedure producing pain and/or distress:**
Five groups were challenged with different organisms in this study. One group was inoculated orally and intranasally with a virulent strain of (b)(4) One group was inoculated intravenously with a virulent strain of (b)(4) One group of dogs was intravenously inoculated with a virulent strain of (b)(4) Another group of dogs was inoculated intravenously with a virulent strain of (b)(4) One group of immunosuppressed dogs was inoculated orally and intranasally with two virulent strains of (b)(4) They then were allowed to develop the signs of the various pathogens.

4. **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.**
These studies were done to demonstrate the efficacy of the experimental vaccines. In order for the studies to be valid it is necessary to demonstrate disease in the control animals. The use of medications would affect the expression of clinical signs in the test animals and adversely affect data interpretation.

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

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

COPY FOR YOUR INFORMATION

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

1. **Species: Canine**

2. **Number of animals achieving Cat. E in this study: 12**

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

The dogs were experimentally infected with either (b)(4) (b)(4) and (b)(4) respectively via intraperitoneal injection, following vaccination to evaluate the vaccine's ability to protect against disease caused by the (b)(4) They were allowed to develop (b)(4) and the signs were observed and recorded.

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

The studies were conducted for product registration in the European Union. The studies were required to evaluate the vaccine's ability to protect vaccinated animals against (b)(4) while the non-vaccinated animals must show clinical signs of the disease. Challenge with (b)(4) may cause severe disease, which will result in a certain degree of pain and distress. Since the study relies heavily on expression of the clinical signs of the disease, treatment with antipyretic, analgesics, non-steroidal anti-inflammatories, corticosteroids or antibiotics for pain and distress would alter the results.

5. **Cite the agency and regulation that requires or supports this procedure.**

The study was conducted to meet the registration requirement for the European Union as per (b)(4)

NOV 24 2004

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

1. **Species: Canine**

2. **Number of animals achieving Cat. E in this study: 57**

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

   The dogs were experimentally infected with (b)(4) following vaccination to evaluate the vaccine's ability to protect against disease caused by the (b)(4) The dogs were infected by the intraperitioneal and subconjuctival administration of a suspension of virulent (b)(4) They were allowed to develop (b)(4) and the signs were observed and recorded.

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

   The literature reports that (b)(4) may be a cause of (b)(4) disease in dogs. The clinical manifestations of experimentally induced (b)(4) however, have not been described. This set of experiments was aimed at determining if possible, whether (b)(4) could be an etiologic agent of clinical disease in dogs. Also it was desired to determine whether vaccination might be of benefit.

   The studies were required also to evaluate whether a prototype vaccine protected vaccinated animals against (b)(4) while the non-vaccinated animals must show clinical signs of the disease. Challenge with some (b)(4) may cause severe disease, which will result in a certain degree of pain and distress. Since the study relies heavily on expression of the clinical signs of the disease, treatment with antipyretic, analgesics, non-steroidal anti-inflammatories, corticosteroids or antibiotics for pain and distress would alter the results.

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

   (b)(4)

   (b)(4)

COPY FOR YOUR INFORMATION

(b)(4) [redacted]

NOV 24 2004

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

1. **Species: Feline**

2. **Number of animals achieving Cat. E in this study: 20**

3. **Explanation of the procedure producing pain and/or distress:**
Cats were anesthetized and small volume of challenge material, containing a virulent strain of (b)(4) known to cause (b)(4) in cats, was administered intranasally. The cats were then allowed to develop clinical signs of the infection so that observations could be made and recorded.

4. **Scientific justification why pain and/or distress could not be relieved.**
This animal study was done for the qualification process of a new feline vaccine. Therapeutic treatments for pain or distress can affect the expression of clinical signs associated with (b)(4) The daily observations of clinical signs are an integral necessity in the outcome of the study that demonstrates the efficacy of the vaccine. Any treatment to alleviate clinical signs would dramatically alter the accurate scoring of study.

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)

(b)(4)

(b)(4)

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

1. **Species: Feline**

2. **Number of animals achieving Cat. E in this study: 40**

3. **Explanation of the procedure producing pain and/or distress:**
Cats were anesthetized and small volume of challenge material, containing a virulent strain of (b)(4) known to cause (b)(4) in cats, was administered intranasally. The cats were then allowed to develop clinical signs of the infection so that observations could be made and recorded.

4. **Scientific justification why pain and/or distress could not be relieved.**
This animal study was done for the qualification process of a new reference vaccine. Therapeutic treatments for pain or distress can affect the expression of clinical signs associated with (b)(4) The daily observations of clinical signs are an integral necessity in the outcome of the study that demonstrates the efficacy of the vaccine. Any treatment to alleviate clinical signs would alter the accurate scoring of study.

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)

(b)(4)

(b)(4)

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

1. **Species: Feline**

2. **Number of animals achieving Cat. E in this study: 31**

3. **Explanation of the procedure producing pain and/or distress:**
Cats were inoculated orally and intranasally with a virulent strain of (b)(4) (b)(4) known to cause 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 introduced another variable into the comprehensive observations of the clinical signs as well as may have modified the duration and severity of the clinical signs. This would not allow for true and accurate measurement of the 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)

(b)(4)

(b)(4)

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

1. **Species: Feline**

2. **Number of animals achieving Cat. E in this group of studies: 37**

3. **Explanation of the procedure producing pain and/or distress:**
Cats were inoculated orally and intranasally with a virulent strain of (b)(4) (b)(4) known to cause the emerging, (b)(4) of the disease. The cats were allowed to develop clinical signs of the infection.

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 introduced another variable into the comprehensive observations of the clinical signs as well as may have modified the duration and severity of the clinical signs. This would not allow for true and accurate measurement of the 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 or support this procedure and study.**

(b)(4)

(b)(4)

(b)(4)

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: 13**

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 (passage) the organism in hamsters. In-vitro culture of (b)(4) reduces the virulence of the organism to an unsatisfactory level. The hamsters were inoculated by an intraperitoneal injection of (b)(4) cultured in the laboratory. When the hamsters became sick they were euthanized and the (b)(4) was harvested under sterile conditions. The (b)(4) will contain (b)(4) with an enhanced ability to cause disease. The (b)(4) (after processing) will be used as a source of challenge material for dogs to evaluate the ability of new vaccines to protect dogs against clinical disease caused by (b)(4) infection.

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: Hamster**

2. **Number of animals achieving Cat. E in this study: 7982**

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

Ten hamsters per serial are vaccinated with (b)(4) given IM. After 14-21 days (product dependent), the hamsters are challenged intraperitoneally (IP) with an appropriate dilution of (b)(4) (b)(4) 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 (b)(4) 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 (b)(4) Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. (b)(4) 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. Attached is part of a presentation given by APHIS-USDA-CVB this past June in which they predict the replacement of hamster testing replacement work to go well into 2007 or longer. FDAH is drafting a proposal in the interim to move some serovars into validated *in-vitro* before then. 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 and is active in AHI/USDA collaborations to expedite the national project.

In 2004, FDAH has been evaluating if intervening prior to death due to the infection for the relief of suffering will affect the outcome of the testing. Studies are on going, yet sufficient data has not been accumulated to make a proposal to the APHIS-USDA-CVB in the way the testing is performed. 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.**

(b)(4) [redacted]

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: 176**

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

Ten hamsters are vaccinated with (b)(4) IM of test vaccine. Thirty hamsters are held for use as controls during the challenge. At 21DPV, all vaccinated hamsters are challenged intraperitoneally (IP) with (b)(4) challenge material. Ten non-vaccinated hamsters are challenged IP with (b)(4) (b)(4) and used as challenge controls. Four groups of five non-vaccinated hamsters are given (b)(4) (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 the infection 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.

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 0579-0036-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-0020 CUSTOMER NO. 1625

FORM APPROVED OMB NO. 0579-0036

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

NOVARTIS ANIMAL VACCINES, INC. (NAVI)
1447 140TH STREET
LARCHWOOD, IA 51241

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.) 06/06/05

FACILITY LOCATIONS*(sites)*

NOVARATIS ANIMAL VACCINES, INC. (NAVI)
LARCHWOOD, IA 51241

NOVARIS ANIMAL VACCINES, INC. (NAVI)
BUCYRUS, KS 66013

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		438	136	72	646
7. Hamsters		5853		3727	9580
8. Rabbits		7	1757		1764
9. Non-Human Primates					
10. Sheep					
11. Pigs		22		6	28
12. Other Farm Animals					
CALVES		47			47
13. Other Animals					
GERBILS	40				

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
		11/23/2004

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

PART 1 - HEADQUARTERS

1. Registration Number: 42-R-0020 / 1625

2/3. Species (common name) & Number of animals used in this study:

Guinea Pigs (72)

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

Clostridium Chauvoei Potency Tests. This procedure is a vaccination/challenge model in which death is the endpoint. In accordance with 9CFR117.4.e animals showing clinical signs of illness due to the test are euthanized to prevent further pain and distress. Tetanus Antitoxin Potency Tests. This procedure is a comparative toxin-antitoxin neutralization test that requires controls to be down and unable to rise as an endpoint for the challenge.

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)

Clostridium Chauvoei Potency Tests. This is a vaccination/challenge model in which control animals must contract the illness, therefore, therapeutic intervention would significantly alter the results of the test. Tetanus Antitoxin Potency Tests. This procedure is a comparative toxin-antitoxin neutralization test that requires controls to be down and unable to rise as an endpoint for the challenge.

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: Clostridium Chauvoei ; USDA APHIS CVB; CFR: 9CFR113.106(c); Tetanus Antitoxin Potency Tests.; USDA APHIS CVB; 9CFR113.451(b)

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

1. Registration Number: 42-R-0020 / 1625

2/3. Species (common name) & Number of animals used in this study:

Hamsters (3727)

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

The procedure is a vaccination/challenge model in which death is the endpoint. In accordance with 9CFR117.4.e. animals showing clinical signs of illness due to the test are euthanized to prevent further pain and 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 Item 6 below)

This is a vaccination/challenge model in which control animals must contract the illness, therefore, therapeutic intervention would significantly alter the results of the test.

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: USDA APHIS CVB; 9CFR113.101(c); 9CFR113.102(c); 9CFR113.103(c); 9CFR113.104(c) CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

1. Registration Number: 42-R-0020 / 1625

2/3. Species (common name) & Number of animals used in this study:

Pigs (6)

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

This procedure is a vaccination/challenge model in which death is the endpoint. In accordance with 9CFR117.c animals showing clinical signs of illness due to the test are euthanized to prevent further pain and 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 Item 6 below)

This is a vaccination/challenge model in which control animals must contract the illness, therefore, therapeutic intervention would significantly alter the results of the test.

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: none CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

is required by law (7 USC 2143). Failure to report according to the regulations can ... under 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: 43-R-0009

CUSTOMER NUMBER: 1399

FORM APPROVED

[redacted]

FEB 11 2005 AR "A"

Midwest Research Inst
425 Volker Blvd
Kansas City, MO 64110

02/17/05

Telephone: (816) -753-7600

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 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 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		32			32
5. Cats					
6. Guinea Pigs		1,060		1,442	2,502
7. Hamsters					
8. Rabbits		10			10
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 anesthetic, 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.E.O. OR INSTITUTIONAL OFFICIAL	[redacted]	DATE SIGNED
		11/11/04

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

NOV 16 2004

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: 43-R-0009

2. Number 2,467 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.

See attached document for complete explaination.

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 FDA CFR 610.10
Pharmacopeial Forum Vol. 29 (4) 2003

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

Relative Potency Test for Anthrax Vaccine is detailed in the Pharmacopeial Forum 29(4) 2003 and has been approved by the FDA. Briefly, Anthrax Vaccine is [redacted] into 12 guinea pigs per dilution. Twenty four unvaccinated guinea pigs allocated to three groups are challenged on the same day as vaccinated guinea pigs, each group with [redacted] The challenge dose for vaccinated guinea pigs contains approximately [redacted] All animals are observed for 10 days post challenge. For a valid test, some of the non-vaccinated animals and any vaccinated guinea pigs not protected by the test article must die in order to confirm the virulence of the challenge organism and to demonstrate the relative potency of the vaccine. This requirement is described in the Pharmacopeial Forum Volume 29 (4) 2003 and is mandated by the FDA. Death of the challenge guinea pigs ensues very quickly, thus there is no evidence of pain or distress during daily clinical health observations. This Relative Potency Test has been designed and validated by sponsor and approved by FDA as the only test on which to base the release of safe and efficacious Anthrax Vaccine for the active immunization against *Bacillus anthracis* of individuals between 18 and 65 years of age.

6.

Agency	FDA	CFR 610.10
	Pharmacopeial Forum	Vol.29 (4) 2003

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.: 12-124

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 47-R-0024
CUSTOMER NUMBER: 1610

FORM APPROVED
OMB NO. 0579-0036

Pfizer Inc
601 W Cornhusker Hwy
Lincoln, NE 68521

05/24/05

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 Attached Listing

COPY FOR [illegible]

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		241		5	246
5. Cats		711		2	713
6. Guinea Pigs		2051			2051
7. Hamsters		17215		5238	22453
8. Rabbits		3691			3691
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 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.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
		11 Nov 04

APHIS FORM 7023
(AUG 91)

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

NOV 16 2004

USDA Annual Report of Research Attachment No. 1
Explanation For Animals Listed In Category E – Aphis Form 7023
For The 2003-2004 Annual Report of Research Facility
No. 47-R-0024

Species: Dogs
Number Reported on Form 7023: 5
Study: Challenge Model Development

The study objective was to [redacted] in dogs. Five of the animals in the study died. Pain relieving drugs were not used in the dogs. Two of the dogs, without recognized clinical signs, were unexpectedly found dead. Previous challenges had been mild. The other three dogs were administered supportive therapy without antibiotics and they succumbed to the challenge. Antibiotics were not administered so that the challenge organisms could be identified on re-isolation from the affected animals. Failure to re-isolate the challenge organism would have required that the study be repeated.

Species: Cats
Number Reported on Form 7023: 2
Study: Vaccine Protection

The study objectives were to [redacted] Feline Immunodeficiency Virus (FIV) by challenging vaccinated and control cats. The two cats were found dead in their cages with no previous signs of clinical illness. Pain relieving drugs were not used in the cats. The cats were submitted to the local veterinary diagnostic laboratory for necropsy. [redacted] The cause of death in the [redacted] cat could not be clearly identified.

Species: Hamsters
Number Reported on Form 7023: 5238
Study: 9CFR 113.101, 113.102, 113.103, 113.104

The study objective was to determine the potency of [redacted] in hamsters as outlined in 9CFR 113.101, 113.102, 112.103, and 113.104. The tests are required by regulation as proof of [redacted] potency in each vaccine produced. Death in this test has been used for many years to indicate lack of protection from [redacted]. Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. The rapid progression of the disease in the hamster makes death intervention difficult. Pathology would likely be impacted by the use of anti-inflammatories. For this reason, neither Pfizer INC nor USDA/CVB-L uses any substance to reduce pain or distress. The impact on length of disease, duration of severity, which occur with use of pain medication, is not known. Use of drugs, therefore, would invalidate the scientific value of the protection endpoint

determined by the test. Lack of confidence in the endpoint would render the test useless in judging vaccine potency.

On April 1, 2004, the USDA-CVB published Notice No. 04-09 (Use of Humane Endpoints in Animal Testing of Biological Products). This publication indicates that animals used in testing of biological products may be treated or humanely destroyed if illness has progressed to a point where death is certain to occur. Pfizer Lincoln is in the process of implementing humane endpointing as part of the (b)(4) testing. Company documents are being updated to incorporate the verbiage outlined in the policy section of Notice No. 04-09. Implementation of the practice will follow those updates with an anticipated completion date of 2nd Quarter 2005.

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

1. CERTIFICATE NUMBER: 52-R-0006
CUSTOMER NUMBER: 507

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

Covance Laboratories Inc
9200 Leesburg Turnpike
Department Of Laboratory Animal Medicine
Vienna, VA 22182

Telephone: (703)-245-2200

NOV 2 2 2004

2. 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 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 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 enesthetic, 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 reas such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	37	1651	134	0	1785
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	55	423	0	478
7. Hamsters	0	15	6	0	21
8. Rabbits	30	217	1268	0	1485
9. Non-human Primates	447	1246	181	20 (see attachment)	1447
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	0	0	0	0	0

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)

DATE SIGNED 11/16/04

(AUG 91)

EC

E. Animals were used on a FDA-mandated sub-lethal irradiation study aimed to develop and characterize the best radioprotective medication. Based on FDA requirements only partial palliative/symptomatic treatment could be provided to animals. Animals were observed more frequently and those in pain/distress were euthanized.

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!

JAN 0 3 2008

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

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

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Emory University
Whitehead Biomedical Research Bldg
615 Michael Street Suite G02
Atlanta, GA 30322

Telephone: (404) -727-7428

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	6	15	100	0	115
5. Cats	0	0	64	0	64
6. Guinea Pigs	0	0	34	0	34
7. Hamsters	0	0	0	0	0
8. Rabbits	0	189	44	0	233
9. Non-human Primates	2000	762	1541	21	2324
10. Sheep	0	7	26	0	33
11. Pigs	0	0	379	0	379
12. Other Farm Animals					
VOLES	0	462	908		1370
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)

NAM

DATE SIGNED 1/04/08

hich is obsolete.)

RAW

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
Briarcliff Campus Building, Emory University
Cardiothoracic Research Labs at Crawford Long Hospital, Atlanta, GA
Yerkes National Primate Research Center, Emory University
Yerkes Field Station, Lawrenceville, GA
Whitehead Memorial Research Building, Emory University

Confidential & Proprietary Information

Summary of Studies (Animal) Listed in Column E

Title: (b)(4)

- 14 [redacted]

Squirrel monkeys are used in drug discrimination studies for studies of (b)(4) (b)(4) (b)(4) In these studies, (b)(4) drugs with differing or unknown profiles of (b)(4) 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 (b)(4) (b)(4) and a placebo in a trial (b)(4) 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 (b)(4) 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 (b)(4) 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 (b)(4) stimulus. [redacted] are never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the (b)(4)

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 (b)(4) compounds studied.

Title: (b)(4)

- 3 R[redacted]

Disorders affecting (b)(4) such as (b)(4) are associated with disrupted sleep patterns and arousal. Rhesus monkeys are used in this study to investigate the cellular mechanism of these sleep disorders and how medications act and can be better used to manage them. Nonhuman primates given the (b)(4) are used as a model of (b)(4) Induction of (b)(4) causes (b)(4) (b)(4) This condition cannot be relieved [redacted] (b)(4) (b)(4) Although the federal reporting requirements only considers the use of anesthetics, analgesics and tranquilizers to relieve pain or distress, it should be noted that (b)(4) a more specific and appropriate intervention, may be used (b)(4) (b)(4) in animals on this study.

Title: (b)(4)

- 4 R[redacted]

Human patients with a wide range of illnesses may exhibit a high rate of depression mediated by activation of the immune system and the release of (b)(4) The latter can exert effects upon the brain leading to altered behavior. For example, about 50% of humans given the (b)(4)

(b)(4) therapeutically develop depression. In these studies, the administration of (b)(4) causes chronic immune activation and a (b)(4) similar to depression in humans. Monkeys given the (b)(4) are used to study how it disrupts brain neurochemistry and to develop treatment interventions. The (b)(4) may also be (b)(4) (b)(4) Potentially animals may also experience heightened sensitivity to painful stimuli and other neurological abnormalities (b)(4) immediately following surgery (b)(4)

(b)(4)

(b)(4)

Exceptions to Regulations and Standards

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: 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 [redacted] monkeys [redacted] Monkeys [redacted] in social isolation for periods of three days after drug administration while [redacted] and its [redacted] are excreted. On a scheduled basis afterwards, these animals are placed in a cage specially designed for [redacted] and [redacted] in a room separated from the other monkeys. Individual 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 for at least 7 days before repetition. 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 [redacted] which telemeter their [redacted] This telemetric approach allows studying sleep behavior in monkeys that are [redacted]. In addition, physical restraint in a chair is done [redacted] facilitate [redacted]

- Title: [redacted]
- Title: [redacted]
- Title: [redacted]

Physical Restraint

Monkeys in these studies are trained to do simple motor tasks such as reaching, depressing a lever, touching a target on a video screen, depressing a key to make a video target appear, or controlling a joystick to move a cursor to a target on a video [redacted]

- Title: [redacted]
- Title: [redacted]
- Title: [redacted]

Physical Restraint and 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. Some animals used under these conditions are in studies of normal control of movement or motion disorders induced by [redacted] Monkeys given [redacted] may be kept in social isolation for periods of three days after drug administration and while [redacted] are excreted. Before and after [redacted] administration, 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 (b)(4) in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for (b)(4) Additionally, the administration of the (b)(4) to induce (b)(4) 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 (b)(4) are 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

- Title: (b)(4)
- Title: (b)(4)
- (b)(4)

B. In the study of (b)(4) studied following injections of (b)(4) The safety and efficacy of [illegible] also will be evaluated. Single or protected contact housing is required after surgery for 6 to 16 weeks to evaluate behavior and

- (b)(4)
- (b)(4)

C. Experiments to test whether (b)(4)
(b)(4)
[illegible] venous catheters; protected contact housing is required during this period to avoid removal of catheters by cagemates.

- Growth regulation of the neurobiology of puberty: 44 rhesus macaques

D. (b)(4)
(b)(4) [illegible] from the group for 48 hours for timed blood collections.

- (b)(4)

E. Infectious disease vaccine development studies may require single housing to prevent disease agent transmission. Some of the studies described here involve the development of a (b)(4) 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 and treatment regimens. 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.

A study testing the effects of (b)(4) 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.

(b)(4) 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 (b)(4)

(b)(4)

(b)(4) 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 to evaluate viral load and safety testing of gene therapy in a hepatitis C study, it is necessary to maintain the animals in metabolism cages. This is due to frequent blood collections and surgical interventions during the initial 4—6 weeks on study.

- Core A: Preclinical trials and pathology (Part of NCVDG Grant: DNA and protein immunogens for SIV/HIV vaccines): 77 rhesus macaques
- Core A: Nonhuman primates (Program Project Grant): 37 rhesus macaques
- New live viral vectors in candidate AIDS vaccines: animal trials core: 44 rhesus macaques
- Cellular immune responses and AIDS pathogenesis: 22 rhesus macaques and 16 mangabeys
- Induction of P vivax, P ovale, P malariae and other plasmodium infections in chimpanzees to obtain large volumes of parasites for malaria vaccine studies: 7 chimpanzees
- Molecular evolution of multiply deleted SIV in vitro: 24 rhesus macaques
- Core C: Primate Studies: 88 rhesus macaques
- Infant immunoprophylaxis against a primate lentivirus: 30 rhesus macaques
- Mechanism of oral SIV transmission: 5 rhesus macaques
- Analysis of thymic function during SIV infection: 6 mangabey, 1 rhesus macaque
- T cell turnover in normal and SIV infected sooty mangabeys: 3 mangabeys
- SHIV macaque model of oral immunization against sexually transmitted HIV: 4 rhesus macaques and 8 pigtail macaques
- Replication defective HIV vaccine: 6 rhesus macaques
- Role of virus specific immunity in primate AIDS: 3 mangabeys, 20 rhesus macaques
- Molecular analysis of antigenic variation in malaria: 17 rhesus macaques
- Malaria, pregnancy and immunophysiopathology: 1 rhesus macaque

- In vivo evaluation of candidate drugs: 11 rhesus macaques
- AIDS & opiates: a monkey model: 20 rhesus macaques
- Combination DNA and attenuated virus vaccine for SIV : 14 rhesus macaques
- Immune modulation of neurotropin in SIV infection: 23 rhesus macaques
- Experimental Inoculations of Macaques with Rotavirus: 6 rhesus macaques, 12 pigtail macaques
- Face Processing in Chimps Using PET: 4 chimpanzees
- Environmental Enrichment of Yerkes Primate Center Animal Colony: 2 rhesus macaques
- Colony Management Support: 131 rhesus macaques (Recently received animals in quarantine)
- Project 3: attenuated listeria vectors as an AIDS vaccine in macaques: 28 rhesus macaques
- Pox virus immunity and DNA/MVA HIP vaccines: 16 rhesus macaques
- Therapeutic vaccine for HIV: 9 rhesus macaques
- Immune modulation of neurotropin in SIV infections: 17 rhesus macaques
- Safety testing of AAV vectors in the liver of hepatitis C virus infected chimpanzees: 4 chimpanzees

F. Studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for human clinical trials in [redacted] (b)(4) (b)(4) Then [redacted] to prevent possible trauma to the surgical wound.

- Use of osteoinductive factors to enhance spine fusion: 10 rhesus macaques
- Use of osteoinductive factors (BMP2)—spine fusion: 3 rhesus macaques

G. (b)(4) [redacted] (b)(4) [redacted] collections, and liver biopsies, as well as physical exams necessitate single cage housing for 45 days.

- Safety evaluation of anti-APO-1/Fas antibody in the chimpanzee: 10 chimpanzees

H. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One proposal is directed towards brain activation studies during [redacted] (b)(4) (b)(4) [redacted] In studies on [redacted] 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 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.

Assessment of specific roles of separate neuronal structures are performed on monkeys to evaluate the brain's response to [redacted] (b)(4)
(b)(4)
[redacted] required for post surgical events until healing has occurred. Implants may require single cage housing to prevent damage to implants in incompatible animals.

- Transition states of drug addiction in nonhuman primates: 12 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: 5 Rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 26 Rhesus macaques
- Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
- Cortical circuitry related to neurotransmission proteins: 2 rhesus macaques
- Analysis of the neuronal microcircuitry basal ganglia: 1 squirrel monkey
- Orbitofrontal limbic ontogeny and early dysfunction: 12 rhesus macaques
- Development of reversible inactivation technique: 2 rhesus macaques
- Development of medial temporal lobe function: 6 rhesus macaques

I. 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: 2 rhesus macaques
- Visual Processing and Smooth Eye Movement: 11 rhesus macaques
- Binocular coordination of eye movements in monkeys: 6 rhesus macaques

J. 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 Rapamycin 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.

- Non-human primate pancreatic islet cell transplantation: 16 rhesus macaques, 8 baboons
- The effect of dosing strategy for LEA29Y on renal allograft survival in rhesus macaques: 23 rhesus macaques
- Activation, apathy, anergy, and apoptosis in transplantation: 6 rhesus
- Transplant Tolerance Project 2: 11 rhesus macaques
- Transplant Tolerance in Non-Human Primates: Costimulation, chimerism and tolerance in transplantation (Project 3): 52 rhesus macaques

K. In this study to evaluate replacement of arteries with vascular grafts, subjects will have aorto-iliac graft implants. Animals are singly housed to permit healing following this major surgery and evaluation of complications. Animals remain on study 1 month following surgery.
    - Evaluation of small vessel prostheses: 20 baboons

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 (b)(4) (b)(4) Monkeys in these studies usually are given (b)(4) 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, isolation housing is only done for a 3 day period immediately after administration of (b)(4) 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 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. 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 restricted, but provided during and after laboratory testing sessions:
   - Title: Basal ganglia discharge patterns in Parkinsonism: 5 rhesus monkeys
   - Title: Influence of subthalamic nucleus on striatal dopamine: 4 rhesus monkeys
   - Title: Pathophysiology of the basal ganglia in Parkinsonism: 5 rhesus monkeys
   - Title: Deep brain stimulation in the Parkinsonian monkey: 6 rhesus monkeys
   - Title: Cortical mechanisms of motor processing: 4 rhesus monkeys
   - Title: Development of gaze-holding abilities: 6 rhesus macaques

2. Short-term physical restraint only:
   - Title: Transition states of drug addiction in nonhuman primates: 12 rhesus macaques
   - Title: Glutamate in Parkinson's disease: 6 rhesus macaques
   - Title: PET neuroimaging and cocaine neuropharmacology in monkeys: 26 rhesus macaques
   - Title: Cocaine use and pharmacotherapy effectiveness in monkeys: 5 Rhesus macaques
   - Title: Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
   - Title: The error signal for postnatal eye growth in the primate: 3 rhesus macaques
   - Title: Emotional and Endocrine Covariates of Macaca mulatto: 48 rhesus macaques
   - Title: Orbitofrontal limbic ontogeny and early dysfunction: 12 rhesus macaques
   - Title: Development of reversible inactivation technique: 2 rhesus macaques
   - Title: Development of medial temporal lobe function: 6 rhesus macaques

Exemptions from Exercise for Dogs

Dogs with an inherited motoneuron disease may be restricted from exercise for 3-4 days while acutely recovering from surgery.

- Title: Functional studies in motoneuron disease: 14 dogs.

Food or Water Restriction of Swine

Swine to undergo survival bowel surgery are restricted from solid food and given an all-liquid diet for 2-3 days prior to surgery in order to fully cleanse the gastrointestinal tract including the lengthy spiral colon.

- Title: Laparoscopic ureteral replacement with reconfigured colon: 1 pig.

is report is required by law (7 USC 2143). Failure to report according to the regulations can sult 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. 01/06/05

Interagency Report Control No.: A1 K. Garland SARS

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 93-R-0189
CUSTOMER NUMBER: 1143

FORM APPROVED
OMB NO. 0579-0036
M. Smith

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Northview Pacific Laboratories, Inc.
551 Linus Pauling Drive
Hercules, CA 94547

Telephone: (510) -964-9000

COPY FOR YOUR INFORMATION

. 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	0	11	40	0	51
5. Cats	0	0	0	0	0
6. Guinea Pigs	87	3041	29	1	3071
7. Hamsters	0	83	0	0	83
8. Rabbits	108	1398	204	7	1609
9. Non-human Primates	0	0	0	0	0
10. Sheep	0	0	0	0	0
11. Pigs	0	25	7	0	32
12. Other Farm Animals	0	0	0	0	0
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 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)

ICIAL

DATE SIGNED 9/30/04

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

OCT - 5 2004

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.

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1. Registration Number: 93-R-0189

2. Number 1 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 used in maximization sensitization testing. This involves intradermal injections of emulsions containing Freunds Complete Adjuvant (FCA) as a necessary part of the initial immune induction procedure. These injections sometimes cause the animals to develop inflammatory lesions. ~~Drugs~~ In this case, the guinea pig was euthanized prior to the end of the test.

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)

Drugs are not used to treat lesions as this would interfere with the purpose of the test

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 ISO 10993-10 CFR

FDA ODE Memorandum #G95-1

OCT 5 2004

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1. Registration Number: 93-R-0189

COPY FOR YOUR INFORMATION

2. Number 7 of animals ~~used in this study~~.

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

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

1. One of two Rabbits on a test became sick. The animal was euthanized. Necropsy indicated the sickness was not likely to be test article-related.

2. Six rabbits were being used to test for eye irritation. The rabbits had an adverse reaction to the test article and were euthanized immediately.

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)

In cases (1) and (2) above, there was no pain or distress anticipated at the start of study. When it occured and the animals were euthanized we changed our electronic records to reflect the change of category.

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 CPSC (Consumer Product Safety Commission) CFR 16 Part 1500

OCT - 5 2004