

UNITED STATES DEPARTMENT OF AGRICULTURE  
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1180

1. REGISTRATION NO.

93-R-0029

Laris

FORM APPROVED  
OMB NO. 0579-0036

MS

ANNUAL REPORT OF RESEARCH FACILITY  
(TYPE OR PRINT)

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

Roche Bioscience  
M/S R2-ITS  
3401 Hillview Avenue  
Palo Alto, CA 94304

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)

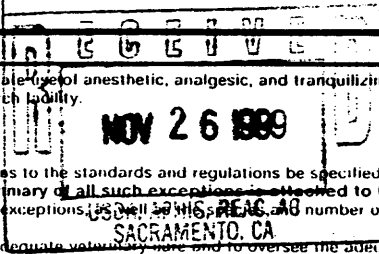
3401 Hillview Avenue, Palo Alto, CA 94303

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	175	402	246	8	656
5. Cats	8	0	61	0	61
6. Guinea Pigs	10	49	102	0	151
7. Hamsters	0	0	0	0	0
8. Rabbits	30	90	34	0	124
9. Non-human Primates	206	118	34	4	156
10. Sheep	0	0	0	0	0
11. Pigs	9	0	29	11	40
12. Other Farm Animals					
13. Other Animals					
Frogs	0	12	17	0	29

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 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 HEADQUARTES RESEARCH FACILITY OFFICIAL  
(Chief Executive Officer or Legally Responsible Institutional Official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL

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

DATE SIGNED

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

Roche Palo Alto

23  
NOV  
99

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

**ROCHE BIOSCIENCE**  
**Registration No. 93-R-0029**  
**Explanation for Category E, APHIS Form 7023**  
**10/1/98-9/30/99**

Roche Bioscience animal research and testing protocols are designed, insofar as is possible, to eliminate pain and distress. In some cases, however, the use of anesthetics, analgesics, or tranquilizing drugs would impair or invalidate test results.

Six dogs may have experienced pain or distress when they were used to evaluate the toxicity potential of new drugs as required by regulatory agencies (i.e., FDA). It was not the intent of the studies to produce pain. For decades, the FDA has required the use of one rodent and one nonrodent species to prove drug safety. Recent references include the Federal Register, August 26, 1996, Vol. 61, #166, pg. 43933 to 43935, and Center for Drug Evaluation and Research Guidance for Industry: M3 Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals, July 1997. Dogs and nonhuman primates are the industry standards for nonrodent, mammalian species.

Eleven pigs, 2 dogs, and 4 nonhuman primates may have experienced pain or distress on the IACUC protocols "Urethral Obstruction Model in Conscious Pigs", "Urethral Obstruction Model in Conscious Dogs", and "Urethral Obstruction Model in Conscious Cynomolgus Monkeys", respectively. Chronic urinary bladder obstruction in humans is due primarily to an enlarged prostate. The large animal model is intended to mimic the chronic human condition, therefore, a surgically implanted obstruction must be present for at least 4-6 weeks before the model is useful. The purpose of this study is to study the disease and develop drugs to prevent symptoms related to involuntary bladder contractions that are caused by a supersensitivity of nerves innervating the bladder. The supersensitivity develops as the result of urine retention and increased voiding pressures that occur over an extended time period (i.e., months). Animals were administered post-surgical analgesics and were closely monitored by the research and veterinary staff. Analgesics alone would not prevent or relieve the discomfort from the urge to urinate, and anesthetics would not be feasible due to the long time period necessary for the model to develop. Sedation was provided to animals that demonstrated more pronounced straining. Animals were euthanized if severe complications arose.

**References:**

1. Speakman, MJ, et al. Bladder Outflow Obstruction – Cause of Denervation Supersensitivity. The Journal of Urology. 138:1461-1466, 1987.
2. Jorgensen, TM, et al. Experimental Bladder Hyperreflexia in Pigs. Urological Research 11:239-240, 1983.
3. Sibley, GNA. An Experimental Model of Detrusor Instability in the Obstructed Pig. British Journal of Urology. 57:292-298, 1985.

**IACUC-Approved Deviations from U.S.D.A. Standards**

Twenty-three dogs were excluded from regular exercise periods for 4-21 days following administration of radioactively-labeled compounds as part of a metabolism study. They were confined to individual metabolism cages to allow collection of excreta. The cage size conformed to USDA standards. During this period, they all received extra attention and human interaction. They were housed in a room with other dogs on the study and were therefore in visual, olfactory, and auditory contact.

Roche Bioscience

Pharma Division

3401 Hillview Avenue  
Palo Alto  
California 94304-9819

2646.doc

