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. 31-R-0117 CUSTOMER NO. 28786

FORM APPROVED OMB NO. 0579-0036

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

WIL RESEARCH LABORATORIES LLC
1407 GEORGE ROAD
ASHLAND, OH 44805
(419) 289-8700

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	100	1280	103	0	1383
5. Cats	0	8	0	0	8
6. Guinea Pigs	0	190	0	0	190
7. Hamsters	NA	NA	NA	NA	NA
8. Rabbits	278	4161	224	11	4396
9. Non-Human Primates	73	716	41	0	757
10. Sheep	0	19	1	0	20
11. Pigs	0	70	1	0	71
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)

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		24 Nov. 2008

(AUG 91)

PART 1 - HEADQUARTERS

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WIL Research Laboratories, LLC

USDA Annual Report- 2008
Reporting Period- October 1, 2007 through September 30, 2008
Facility Registration Number: 31-R-0117
Customer Number : 28786

2008 Category E Animals-

Eleven (11) Rabbits were placed in Category "E"

A total of 12 rabbits were involved in an oral gavage pilot toxicokinetic study used to select appropriate dosage levels for embryo fetal development toxicity studies. Five (5) Rabbits may have experienced pain and/or distress for which anesthetic, analgesic or tranquilizing drugs were not used. With the exception of these five animals the remaining seven were not noted with signs of pain and/or distress. The test article, a small molecule inhibitor of the family of Janus kinases, is currently being evaluated in the clinic for the treatment of rheumatoid arthritis. Part of the evaluation is to conduct studies in accordance with the International Conference on Harmonisation (ICH) Tripartite Guideline on Detection of Toxicity to Reproduction for Medicinal Products, Federal Register, September 22, 1994, Section 4.1.3 (Study for effects on embryo-fetal development); typically, studies involving both a rodent species and a non-rodent species (usually rabbit) are required for evaluation. Prior to the conduction of the present study, the test article had never been tested in rabbits. The objective of this study was to generate enough toxicokinetic data, with using as few animals as possible for achieving meaningful information, to select dosage levels for the ICH 4.1.3 embryo/fetal development toxicology studies in the New Zealand White rabbit. The study consisted of 12 non-pregnant rabbits at four different dose levels that received test article by oral gavage for 5 consecutive days. Five animals were characterized as "E". Three animals in the high dose group and 1 animal in the middle-high dose group, that may have experienced pain and/or distress, were dosed for 1 consecutive day. Another animal in the middle-high dose, that may have experienced pain and/or distress, was dosed for 2 consecutive days. Pre-dose and 1 hour post-dose clinical observations for these animals were conducted daily. Characterization criteria "E" was selected for these 5 animals because of clinical observations such as gasping, labored respiration and prostrate. Anesthetic, analgesic or tranquilizing drugs were considered for use for these 5 animals, however, their use would have interfered with the scientific objectives of this pilot study (which was to assess potential maternal toxicity in non-pregnant rabbits prior to initiating the ICH guideline studies).

A total of 3 rabbits were involved in an acute eye irritation study used to determine the primary ocular irritative potential of the test article in albino rabbits. The three (3) rabbits may have experienced pain and/or distress for which anesthetic, analgesic or tranquilizing drugs were not used. An initial animal was dosed and had a small area of scattered or diffuse ocular opacity and slight to moderate swelling and redness were noted. No signs of pain or distress were noted and all positive signs of irritation subsided within 7 days. Thus the remaining two animals were dosed. These animals displayed a stronger reaction to the test article with larger areas (still less than one half the corneal surface) of discernible opacity, iritis and significant swelling, redness and discharge. No signs of pain or distress were recorded and the irritation subsided. All

2008 Category E Animals-
(continued)

animals gained weight over the course of the study so there was no apparent disruption in their eating behavior. The study was conducted in order to provide information on the health hazards likely to arise from a short-term exposure to the test article by the ocular route. The test article was a resin used in and fabric dipping and processing and; therefore, it has a high possibility for accidental ocular exposure in humans. At this time, other than a few *in vitro* methods used to screen for corrosive materials, there are no acceptable alternatives for the use of animals for evaluating and categorizing ocular irritation potential. The rabbits displayed no signs of pain or distress that would have prompted consideration of the use of anesthetic, analgesic, tranquilizing drugs or euthanasia. The study was conducted in accordance in accordance with Environmental Protection Agency (EPA) Office of Prevention, Pesticides and Toxic Substances (OPPTS) guideline 870.2400 (1998), Organisation for Economic Cooperation and Development (OECD) Guidelines for Testing Chemicals, Section 405 (2002), and the European Union (EU) Guideline in the Official Journal of the European Communities [92/69, Annex V, B5 (1992)].

Another study with a total of 3 rabbits were involved in an acute eye irritation study used to determine the primary ocular irritative potential of the test article in albino rabbits. Two (2) rabbits may have experienced pain and/or distress for which anesthetic, analgesic or tranquilizing drugs were not used. An initial animal was dosed and showed no signs of irritation other than very slight redness and swelling that subsided within 72 hours. Thus the remaining two animals were dosed. These animals displayed a stronger reaction to the test article with small areas of scattered or diffuse opacity and significant swelling, redness and discharge up to 96 hours after dosing. All positive signs of irritation subsided by study day 7. No signs of pain or distress were recorded. All animals gained weight over the course of the study so there was no apparent disruption in their eating behavior. The study was conducted in order to provide information on the health hazards likely to arise from a short-term exposure to the test article by the ocular route. The test article was a fungicide and; therefore, it has a high possibility for accidental ocular exposure in humans. At this time, other than a few *in vitro* methods used to screen for corrosive materials, there are no acceptable alternatives for the use of animals for evaluating and categorizing ocular irritation potential. The rabbits displayed no signs of pain or distress that would have prompted consideration of the use of anesthetic, analgesic, tranquilizing drugs or euthanasia. The study was conducted in accordance in accordance with Environmental Protection Agency (EPA) Office of Prevention, Pesticides and Toxic Substances (OPPTS) guideline 870.2400 (1998), Organisation for Economic Cooperation and Development (OECD) Guidelines for Testing Chemicals, Section 405 (2002), and the European Union (EU) Guideline in the Official Journal of the European Communities [92/69, Annex V, B5 (1992)].

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IACUC approved reportable exceptions to the Animal Welfare Act

77 Beagle dogs used in Telemetry Cardiovascular Assessment studies were implanted with DSI telemetry implants and exempted from exercise during the 14 day surgical recovery period. These animals were given regular opportunity for exercise and socialization prior to and after a 14 day surgical recovery. During the surgical recovery period, dogs were given daily contact and interactions with the technical staff as well as visual, auditory and olfactory stimuli from other dogs in the room.

6 Beagle dogs were used in a single-dose pharmacokinetic and bioavailability study. This study required that fecal samples be collected periodically through 84 hours post-dosing and urine samples collected through 72 hours post-dosing. These dogs were exempted from exercise by IACUC approval only during the specified collection times otherwise the animals were given regular opportunity for exercise and socialization in accordance with Standard Operating Procedures and the Animal Welfare Act.

3 Beagle dogs were used in a study to determine the routes of excretion and mass balance of a radio-labeled test article. This study required that fecal and urinalysis samples be collected periodically through 120 hours post-dosing. These dogs were exempted from exercise by IACUC approval only during the specified collection times otherwise the animals were given regular opportunity for exercise and socialization in accordance with Standard Operating Procedures and the Animal Welfare Act.