This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 21

See attached form for additional information.

Interagency Report Control No.

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 48-R-0004
CUSTOMER NUMBER: 1400

FORM APPROVED
OMB NO. 0579-0036

Bayer Corp. Agric. Division, Toxicology
Bayer Research Park
(b)(2)High, (b)(7)(F)
Stilwell, KS 66085

Telephone: (913) -433-5278

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

FACILITY LOCATIONS (Sites) - See Atached Listing

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

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	21	248	65	10	323
5. Cats					0
6. Guinea Pigs	14	54	66	0	120
7. Hamsters					0
8. Rabbits					0
9. Non-human Primates	1	87	25	0	112
10. Sheep					0
11. Pigs	0	7	0	0	7
12. Other Farm Animals					0
13. Other Animals					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)

(b)(6),(b)(7)(c)

FICIAL

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

(b)(6),(b)(7)(c)

DATE SIGNED

11/25/08

6 2s (OCT 88), which is obsolete.)

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Column E Explanation

1. **Registration Number:** 48-R-0004

2. **Number of animals used in this study:** Ten in column E

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

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

The procedure was a 90-day toxicology and toxicokinetic study with a 45-day recovery period. An escalating dose design was used, and the highest dose produced clinical signs of tremors and seizure.

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 objective of the study was to determine the toxicity and toxicokinetic profile of the test article following oral administration for 90 days, and to determine if delayed toxicity and/or recovery occur after a recovery period of 45 days. The pharmacological signs associated with the drug could not be treated as it would interfere with characterizing the toxicity of the drug and whether any toxicity was delayed or reversible.

The study was conducted per the requirements of FDA 21 CFR 312.23 as follows: (a) IND content and format; (8) Pharmacology and toxicology information: Adequate information about pharmacological and toxicological studies of the drug involving laboratory animals or in vitro, on the basis of which the sponsor has concluded that it is reasonably safe to conduct the proposed clinical investigations"; (ii) Toxicology: "an integrated summary of the toxicological effects of the drug in animals..." and "....the description is to include the results of acute, subacute and chronic toxicity tests...".

The study was conducted per ICH M3 Nonclinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals. This guideline requires "A characterization of toxic effects with respect to target organs, dose dependence, relationship to exposure, and potential reversibility. The nonclinical safety studies.....should be adequate to characterize potential toxic effects under the conditions of the supported clinical trial".

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 **CFR:** 21 CFR 312.23 (a)(8)(ii)

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