51 R 0025

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: 51-R-0025

2. Number 4 of animals used in this study.

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

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

The rabbits were given an intravenous infusion (ear vein catheter) of a potential cancer chemotherapeutic drug to get some base line data on potential adverse side effects as a result of the infusion. Preliminary data in rats involving bolus administration were used to determine the range of doses to use in the rabbits (based on body surface area). This protocol was the first opportunity to study the effects resulting from an intravenous infusion. Rabbits were given a continuous infusion of the drug until either adverse effects were seen or the total dose given. Effects seen at the high infusion rates included muscle tremors/weakness, labored breathing, pupillary dilation, salivation. If side effects were noted, the infusion was stopped immediately. Each subsequent rabbit was given a lower dosage rate until no adverse effects were noted.

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 scientific purpose of the protocol was to determine if a continuous intravenous infusion of the chemotherapeutic drug would produce adverse side effects when given to a rabbit. Thus, it was necessary that clinical signs be allowed to occur. However, once signs did appear clinically, the infusion was stopped and the rabbit allowed to recover. Analgesics, sedatives or other such drugs could not be used since they would mask any clinical signs. Besides looking for adverse signs the investigator wanted to determine a potentially safe dosage rate and so several infusion rates needed to be tested. Four rabbits were used because each rabbit was used only once. If and only if the results of these in-vivo tests were promising would the investigator then pursue FDA approval.

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 re... 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 re... dle for addition... ...rmation

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)

-92

1. REGISTRATION NO. ~~51-R-0032~~ 51-R-0032

FORM APPROVED
OMB NO 0579-0036

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

Biocon, Inc.
15801 Crabbs Branch Way
College Park Campus
Rockville, MD 20855
Status: Active

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~~

DEC 01 1999

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		65	121	ϕ	186
7. Hamsters		1419	ϕ	ϕ	1419
8. Rabbits		159	95	133	387
9. Non-human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
Ducks		6	ϕ	ϕ	ϕ

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)

(b)(6), (b)(7)(C) 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
[redacted]	[redacted]	11/30/99

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

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