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-0002
CUSTOMER NUMBER: 1459

FORM APPROVED
OMB NO. 0579-0036

University Of Kansas
Animal Care Unit
B054 Malott Hall
Lawrence, KS 66045

Telephone: (785) -864-5587

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		4			4
5. Cats					
6. Guinea Pigs					
7. Hamsters					
8. Rabbits			251	4	255
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 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)

NOV 24 2008 ✓

(b)(6), (6)(7)(C)	NAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print) (b)(6), (6)(7)(C)	DATE SIGNED 11/20/08

APHIS FORM 7023 (Replaces VS FORM 18-23 (OCT 88), which is obsolete.)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

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: **48-R-0002 / 1459**

2. Number of animals used in the study: **4**

3. Species (common name) of animals used in the study: **Rabbits**

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

One study on rabbits involves the injection of LPS (endotoxin) a model of sepsis. While this is not painful it may potentially result in distress to the animals. The experiment is intended to study the treatment of sepsis with a drug, AK-262. The major objective of this project is to confirm results pertaining to protective effects of the compound that was designed to bind to bacterial lipopolysaccharides (LPS) and neutralive them in a panel of vitro assays as well as in a murine model of LPS-induced septic shock. The results we have obtained so far indicate that this compound is highly efficacious, and yet is without discernable toxicity.
Extensive in vitro studies such as inhibition of LPS-stimulated nitric oxide production (murine J774 cells), cytokine inhibition (TNf-alpha, IL-1 beta, IL-6, IL-8; in human blood ex vivo), inhibition of LPS-stimulated p38 MAP kinase (human neutrophils), inhibition of LPS-stimulated NF-kappa-B (human HEK-239 cells) all indicate excellent LPS-neutralizing activity of the compound. Futhermore, extensive in vivo data (CF-1 mouse) confirm that the anti-lipopolysaccharide activity of AK-262 is highly effective. We need to demonstrate that AK-262 effective in an animal model that does not need D-galactosamine sensitization to the effects of lipopolysaccharide? Animals that are highly sensitive to lipopolysaccharide are humans, rabbits, and horses. Mice are relatively resistant. Mice, therefore, need to be sensitized to the lethal effects of the toxin by administering D-galactosamine. Rabbits are a feasible model in this context to obtain confirmatory pre-clinical data.
In animals receiving the test compound (AK-262), it is possible that some animals may become sick and may therefore need to be euthanized before the end of the one-week observation period. All animals will be monitored twice daily for significant clinical signs including listlessness and or lethargy, dyspnea, altered consciousness, seizures, anorexia, and diarrhea. Any animal that becomes excessively ill will be euthanized as described above, after consultation with the attending veterinarian.

5. Provide scientific justification why pain and/or distress could not by relieved. State methods or means to determine that pain and/or distress relief would interfere with test result. (For Federally mandated testing, see Item 6 below)

We use non-lethal doses of lipopolysaccharide that induces a measurable pyrogenic (temperature) response (0.6-1 deg. Celsius). The pyrogenic response in rabbits is a test that is commonly used in the validation of almost any pharmaceutical preparation for parenteral use. The use of any concomitant NSAIDs or antipyretics will obtund the pyrogenic response, thus completely invalidating the assay. This is the reason that we do not propose to use analgesics or antipyretics.

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_____