

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE  <b>ANNUAL REPORT OF RESEARCH FACILITY</b> ( TYPE OR PRINT )	1. CERTIFICATE NUMBER: 33-R-0029 CUSTOMER NUMBER: 603	FORM APPROVED OMB NO. 0579-0036
University Of Illinois At Urbana-Champaign 1 Observatory Building 901 S. Mathews Urbana, IL 61801  Telephone: (217)-333-2564		

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 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 animal 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 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 reas such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E )
4. Dogs		171	382		553
5. Cats	39	111	174		324
6. Guinea Pigs		6			6
7. Hamsters					
8. Rabbits		68	24		92
9. Non-human Primates					
10. Sheep		67	7		74
11. Pigs		745	143	64	952
12. Other Farm Animals					
Goats		6			6
13. Other Animals					
Opossum		65			65
Horses		52			52
Cattle		53	9		62

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 rest 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 )		
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)	11-25-2008

MP



### 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: 33-R-0029

2. Number 10 of animals used in this study.

3. Species (common name) Chinchilla of animals used in the study.

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

Intraperitoneal injection of anesthesia will cause minor pain.

Transbullar injection of *P. aeruginosa* into the middle ear cavity of chinchilla will cause minor pain.

Chinchilla with middle ears infected with *P. aeruginosa* may develop clinical signs include loss of balance, decreased activity, hunched posture, ruffled fur. Animals who are in severe distress (agonal or unable to feed and drink water) will be immediately euthanized.

The animals will be observed four times a day (6 am, noon, 6pm and midnight) from inoculation to euthanizing. Animals meeting the euthanasia criteria (agonal or unable to feed and drink) will be immediately euthanized by carbon dioxide asphyxiation using compressed gas as the CO<sub>2</sub> source, or by intraperitoneal injection of sodium pentobarbital (200 mg/kg body weight).

Four animals inoculated with *P. aeruginosa* developed clinical signs of illness as outlined above. The veterinary staff was contacted immediately for each reported illness, the animals were examined, and the animals were euthanized immediately.

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).

No analgesics will be administered to the animals used in all these studies. The primary reason for not giving analgesics in our studies is that these drugs alter or inhibit the immune reactions we wish to study and would reduce the value of those studies. For example, it is well known that the morphine analogs and endorphins have a significant effect on immune responses as well as regional blood flow and even outcome following injury. In mice phagocytic function of *Version 2-2006* Page 8 of 17 macrophages and polymorphonuclear cells are clearly reduced by morphine. Lymphocyte proliferation, a typical study endpoint in trauma studies, is reduced by morphine. Morphine acts to suppress the immune system, and results in accelerated death in an experimental model of sepsis. Furthermore, naloxone, an antagonist of the morphine-like alkaloids, improves survival in shock. The morphine derivative, buprenorphine, was shown to reduce the serum levels of TNF caused by injection of the bacterial cell wall component LPS by 50%. Buprenorphine has also been shown to activate mast cells, decrease liver weight, induce apoptosis, decrease corticosterone levels, and increase the incidence of pneumonia in experimental rodents. Buprenorphine, may be somewhat less immunosuppressive than morphine, as it has been used to study lymphocyte function. However, in this study, no control to test the effect of buprenorphine on trauma induced lymphocyte proliferation was conducted.

References:

**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: **33-R-0029**
2. Number 64 of animals used in this study.
3. Species (common name) Pigs of animals used in the study.
4. Explain the procedure producing pain and/or distress.

The experiment required a challenge with porcine reproductive and respiratory syndrome virus (PRRSV). At three weeks of age, pigs were divided into blocks of 4 pigs each based on litter of origin, body weight and gender and randomly assigned to one of the four treatments. The four treatments were (1) standard diet with not inoculation of PRRSV, (2) standard diet plus 0.2% of BioMos with no inoculation of PRRSV, (3) standard diet with inoculation of PRRSV, and (4) standard diet plus 0.2% of BioMOs with inoculation of PRRSV. The pigs were inoculated intranasally with 5ml of  $1 \times 10^5$  50% tissue culture infective dose (TCID<sub>50</sub>) of live PRRSV (strain ATCC VR-2385).

Pigs were checked twice a day for any signs of pain and distress (like labored breathing, accented abdominal respiration, lethargy, and rough hair coat). No problems arose that would have required notification of the DAR veterinary staff or euthanasia.

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 purpose of the experiment was to determine whether a feed additive can improve pigs' resistance to a viral disease that is important and pervasive in the swine industry. The prominent clinical signs of the disease in young pigs are fever, reduction in feed consumption, and respiratory signs. The only way to determine whether the treatment ameliorated these signs was to allow the disease to run its course.

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 \_\_\_\_\_

1. Fox JL, Opioids appear to suppress immune system responses. *ASM News* 1999;65:8-9
2. Gungor M, Genc E, Sagduyu H, et. al. Effect of chronic administration of morphine on primary immune response
3. Hendrickson M, Shelby J, Sullivan JJ, et al. Naloxone inhibits the in vivo immunosuppressive effects of morphine and thermal injury in mice. *J. Burn Care Rehab.* 1989;10:494-8
4. Sibinga NES, Goldstein A., Opioid peptides and opioid receptors in cells of the immune system. *Ann. Rev. Immunol* 1988;6:219-49
5. Tubaro E, Borelli G, Croce C, et. al. Effect of morphine on resistance to infection. *J. infect. Dis.* 1983;148:656-66
6. Houghtling RA, Mellon RD, Tan RJ, Bayer BM. Acute effects of morphine on blood lymphocyte proliferation and plasma IL-6. *Ann N. Y. Acad. Sci.* 2000; 917:771-777
7. Roy S, Cain KJ, Charboneau RG, Barke RA. Morphine accelerates the progression of sepsis in an experimental sepsis model. 1998; 437:21-31
8. Jobin N, Garrel DR, Bernier J. Increased burn-induced immunosuppression in lipopolysaccharide-resistant mice. *Cell Immunol* 2000; 200:65-75
9. Piersma FE, Daeman MARC, vd Bogaard AEJM, Buurman WA. Interference of pain control employing opioids in in vivo immunological experiments. 1999; 33:328-333
10. Van Loveren H, Gianotten N, Hendricksen CF, Schuurman HJ, Van der Laan JW. Assessment of immunotoxicity of buprenorphine. *Lab. Anim.* 1994; 28:355-363.

Non-steroidal analgesics block production of prostaglandins , which play a role in the immunosuppression seen in burns. The nonsteroidal analgesic indomethacin, with or without interleukin therapy has been shown to improve survival and reduced leukocyte hyperactivity in burn and sepsis models. Since the principle objective of our studies relates to sepsis induced alterations in immune function and the ability of treatment regimens to improve these functions, these analgesic drugs would clearly influence the results of our study.

#### References

1. Santangelo S, Shoup M, Gamelli RL, Shankar R. Prostaglandin E2 receptor antagonist (SC-19220) treatment restores the balance to bone marrow myelopoiesis after burn sepsis. *J. Trauma* 2000; 48:826-831
  2. Strong, VE, Mackrell PJ, Concannon EM, Naama HA, Schaefer PA, Shafeton GW, Stapelton PP, Daly JM. Blocking Prostaglandin E2 after trauma attenuates pro-inflammatory cytokines and improves survival. *Shock* 2000, 14:374-379.
  3. Horgan PG, Mannick JA, Dubravec DB, Rodrick ML. Effect of low dose recombinant interleukin 2 plus indomethacin on mortality after sepsis in a murine burn model. *Br. J. Surg.* 1990. 77:401-404
  4. Latter DA, Tchervenkov JI, Nohr CW, Christou NV, The effect of indomethacin on burn induced immunosuppression. *J. Surg. Res.* 1987. 43:246-252.
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 \_\_\_\_\_