

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 0180-00A-AN

*A. G. H. Garland & Son
A. Antunes
01/24/05*

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 93-R-0435
CUSTOMER NO. 9194
FORM APPROVED OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)
UNIVERSITY OF CALIFORNIA, LOS ANGELES
[REDACTED]

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)	
[REDACTED]	

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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 (Cois. C + D + E)
4. Dogs			6		6
5. Cats			4		4
6. Guinea Pigs	99		38	702	740
7. Hamsters					
8. Rabbits	8	415	252		667
9. Non-Human Primates		4	19		23
10. Sheep				2	2
11. Pigs			215	18	233
12. Other Farm Animals					
13. Other Animals					
Chinchillas			15		15

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 [REDACTED]	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print) [REDACTED]	DATE SIGNED 11/04/2005
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1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Sheep (2)

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

Hypoxia and the control of fetal breathing.

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 POTENTIAL distress of hypoxia cannot be relieved by anesthetics, analgesics or tranquilizers because these pharmacologic agents alter the physiologic responses that are being studied. The objective of this study is to determine the mechanism by which hypoxia inhibits fetal breathing movements. These studies may be relevant to sudden infant death syndrome, sleep apnea and the general control of respiration.

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: None

CFR:

Approval Status:

Approved/Disapproved By:

Date:

Disapproved Reason:

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1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Guinea Pigs (702)

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

1) 612 Guinea Pigs: Infection with *M. tuberculosis*. 2) 90 Guinea Pigs: Infection with *Leptospira*.

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)

1) The only medications that could possibly relieve any discomfort would be anti-tuberculosis antibiotics. Treating the animals with antibiotics would completely defeat the purpose of the experiment, which is to assess the capacity of new compounds to serve as antibiotics alone or in combination with conventional antibiotics. Guinea pigs infected with *M. Tuberculosis* develop disseminated disease that is manifested by anorexia and weight loss. Animals are weighed daily to monitor progression of the disease, and euthanized immediately if they become moribund. 2) The primary reason for inclusion of animals in category E is to provide a source of infected tissue from which *Leptospira* can be extracted and characterized. The use of any pain/distress/discomfort relieving methods will interfere with the host environment and either inhibit the growth of *Leptospira* in vivo or result in *leptospira* in inaccurate results for the development of a suitable vaccine. Animals are euthanized immediately if they appear moribund or if weight loss reaches 10%.

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: None

CFR:

Approval Status:

Approved/Disapproved By:

Date:

Disapproved Reason:

1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Pigs (18)

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

The technique is to stop the circulation, either with normal temperature (sudden death), or with low body temperature (using a heart lung machine to lower temperature) simulating stroke with periods of no brain blood flow. Placement of venous and/or arterial cannulas.

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)

This study attempts to determine the extent of brain injury after circulatory arrest. Local anesthesia injections (i.e., Marcaine) are administered instead of systemic buprenorphine for postoperative pain relief following placement of venous and/or arterial cannulas. The only invasive procedure is catheter placement. The protocol is Pain Category E, as this provides the coverage needed to discover the effects of the stroke like end point. As described this is without pain, and use of local anesthesia will continue. The reason for withholding global agents is related to clinical events whereby only local pain follows groin incisions. Animals receive supportive care after surgery, continuously for the first 24 hours, thereafter, depending on clinical status of the animal, at least daily until euthanasia.

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: None

CFR:

Approval Status:

Approved/Disapproved By:

Date:

Disapproved Reason:



University of California Los Angeles
Office of the Campus Veterinarian
Division of Laboratory Animal Medicine
David Geffen School of Medicine
Accredited by AAALAC, Int'l. since 1967

Box 957336, Los Angeles, CA 90095
310.794.2571

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93-K-0.435

December 21, 2005

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INFORMATION

Kathleen Garland, VMO
Supervisory Animal Care Specialist
Western Region, Animal Care

Dear Dr. Garland,

The following expanded explanations regarding Category E protocols are presented for your review:

Sheep

#4 - Lambs are placed in a sling and their nose placed inside a standard anesthetic mask. After a 5-10 minute control period of stable ventilation, the fraction of inspired O₂ (FIO₂) will be lowered from 0.21 to 0.07 for 15 minutes, which will be followed by a 10 minute recovery period. Carbon dioxide will be added to the gas mixture to keep PaCO₂ within 1-2 Torr of control values. Various experimental drugs will be administered, direct electrical stimulation of brain areas will be performed, and arterial and venous blood samples will be collected during the period of reduced oxygen. The catheters for bloods collection and the guide cannulas for electrical stimulation of brain areas will be implanted under surgical anesthesia several days prior to the testing period.

#5 - The potential distress of reducing the oxygen content of inhaled gas from normal air (0.21) to lower concentrations cannot be relieved by any anesthetic or sedative/tranquilizer, since all of these drugs have a direct effect on respiration, heart rate, blood pressure, or all of the above. The goals of the experiment could not be met if these drugs were administered.

Guinea Pigs

#4 - 1) 612 Guinea Pigs: Infection with M. Tuberculosis. Guinea pigs are immunized with a vaccine. The route of immunization is intradermal (ID), intramuscular (IM), or subcutaneous (SQ). In some experiments, guinea pigs are boosted with one or more M. tuberculosis extracellular proteins, at various intervals after the initial immunization. At ~10 weeks, the guinea pigs are skin-tested for a delayed-type hypersensitivity (DTH) response and then challenged with an aerosolized dose of M. tuberculosis. 2) 90 Guinea Pigs:

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Infection with *Leptospira*. Guinea pigs will be experimentally infected by intraperitoneal (IP) injection of a 500ul volume of culture which contains 10^3 , 10^5 or 10^7 *Leptospira*. Before injection, the injection site of the guinea pig will be made aseptic by swabbing with 70% ethanol.

#5 - 1) The only medications that could possibly relieve any discomfort from Tb would be anti-tuberculosis antibiotics. Treating the animals with antibiotics would completely defeat the purpose of the experiment, which is to assess the efficacy of a vaccine. In the rare event that an open sore/necrotic skin lesion should occur as a result of the BCG vaccine or skin test, and the guinea pig was in pain/distress, veterinary advice would be sought and topical analgesics could be applied. Guinea pigs infected with *M. Tuberculosis* develop disseminated disease that is manifested by anorexia and weight loss. Animals are weighed daily to monitor progression of the disease, and euthanized immediately if they become moribund. 2) The primary reason for inclusion of animals in category E is to provide a source of infected tissue from which *Leptospira* can be extracted and characterized. The use of any pain/distress/discomfort-relieving methods will interfere with the host environment and either inhibits the growth of *Leptospira* in vivo or results in *leptospira* responding to host conditions not normally encountered during infection which in turn results in inaccurate results for the development of a suitable vaccine. *Leptospira* can be grown in the lab. However, the *leptospira* that grows in the lab is very different than the *leptospira* that grows in an infected animal. A suitable vaccine can only be made using the *leptospira* that grows in the infected animal. Overall, the general goal of these experiments is to infect animals, from which the *leptospira* can be recovered. They will then be characterized in order to develop a vaccine.

Pigs

#4 - Two procedures are used to produce cardiac arrest-induced stroke. The first is induction of fibrillation by way of electrical stimulus (normothermic), and the second is hypothermia by way of lowering the temperature of circulating blood. Both procedures are done with the pig anesthetized with isoflurane and connected to a heart/lung machine via venous and arterial catheters in the inguinal area. Following the circulatory event, the pigs are taken to the MRI unit for a brain scan to determine the extent of the lesion(s).

#5 - Induction of stroke could cause motor deficits or seizures. In this project, the pig is monitored continuously for 24 hours following the stroke induction by laboratory staff, and then euthanized. Seizures (which have not occurred to date) would be controlled with diazepam. Motor deficits severe enough to impair normal food and water consumption require intravenous fluid therapy. Analgesia is provided at the catheter insertion site via bupivacaine (Marcaine) injection.

The goal of this study is to 1) distinguish transient from permanent brain damage via MRI imaging, and 2) determine the efficacy of controlled reperfusion to prevent "reperfusion injury". Administration of opiates or non-steroidal anti-inflammatory agents (NSAIDS)

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could alter the normal inflammatory response to ischemia, as well as the leucocyte response involved in reperfusion injury.

I hope this clarifies the previously provided information. Please feel free to contact me if you need further information or clarification.

Sincerely,



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Cc:



DEC 30 1985

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 93-R-0016

FORM APPROVED
OMB NO. 0579-0038

CUSTOMER NUMBER: 1189

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

Los Angeles Biomedical Research Institute
L.A. Biomed
1124 West Carson Street
Torrance, CA 90502

Telephone: (310)-222-3601

Andreas
COPY

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)

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4. Dogs		187	19		206
5. Cats					
6. Guinea Pigs					
7. Hamsters					
8. Rabbits		6	533		539
9. Non-human Primates					
10. Sheep			134		134
11. Pigs			44		44
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

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(Chief Executive Officer or Legally Responsible Institutional Official)

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

DATE SIGNED

10/11/05

OCT 17 2005



LABioMed

Los Angeles Biomedical
Research Institute 11/06/05
at Harbor-UCLA Medical Center #2

1124 West Carson St.
Torrance, CA 90502

www.LABioMed.org

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Facility Locations

(b)(7)f, (b)(2)High

Approved Variance to Regulations

A variance has been issued by the Animal Care and Use Review Committee on September 15, 2005, to house sheep in metabolic cages. The metabolic sheep cages have a floor space of 11 square feet, this is 4 square feet less than the recommendation. These cages are used for sheep with chronic catheters in place generally both fetal and maternal catheters. The animals need to be confined to a safe, clean environment because of the catheters. The animals can move freely in the cages and can turn around. The animals are housed in the metabolic cages for less than two weeks

OCT 17 2005