University of Washington
Animal Care Committee

ORIGINAL RECEIVED AUG 21 2000 BY:

Project # 2409-68

Request for Significant Change of Animal Use Protocol

*** Please type-handwritten forms will be returned ***

Principal Investigator/Project Director: **Morton, William R.**
Department: **Primate Center** Faculty Title: **Professor, Comparative Medicine**
Project Title: **Evaluation of an osteoinductive material in nonhuman primate osteopenic vertebrae**
Project Dates: **6/21/00** to **6/20/01** Funding Source(s): Commercial

For your information, a list of examples of significant changes is available in the Department of Comparative Medicine Information Manual. This list is not exhaustive, but illustrates the type of changes which require Animal Care Committee approval. To receive a copy of the Information Manual please call the Animal Use Training Coordinator (616-6849). Information on significant changes may be directed to the ACC Coordinator (543-9678).

- For addition of new personnel, submit a "Request for Addition of New Personnel" form.
- If you are requesting additional animals, state the number and species requested and provide the method used to determine the number of animals. Use additional pages as needed.
- For changes in animal use procedures, provide a detailed description of the change(s), being careful to include all required information (use additional pages as needed). Please refer to a Project Review Form for New Projects, to determine the required information.

Certification Statement

I certify that the original Project Review Form in conjunction with this Significant Change, accurately describes all aspects of the proposed animal usage. I further certify that the use is not unnecessarily duplicative. I accept responsibility that all personnel working on the project will adhere to the regulations regarding the humane treatment of laboratory animals and will receive proper training as required by the ACC. I will obtain approval prior to instituting any other significant changes in the project. I understand that the approval is not final until I receive notification of such in writing, and that the ACC can require changes to the protocol. I understand that approval of projects is for a maximum of one year from the date of ACC approval of the original submission, and that approval of the significant changes submitted on this form will not change the date of the annual renewal.

Signature of P.I. _____ Date Aug. 21, 2000

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: II CTC: SEP 1 2000
Comments: _____

Initial Reviewer: _____ Review Date: 8/30/00
Date Approved by ACC: SEP 6 2000 (Annual renewal date of project is not changed.)

PRF Revised 1998

University of Washington
Animal Care Committee

MAY 17 2000

2409-68
PRF-1

Animal Care Committee

PROJECT REVIEW FORM

Please check one: ☒ This is a new project or ☐ This is a 3-year renewal of ACC Protocol # _____

Principal Investigator/Project Director: **Morton, William R.**
Department: **Primate Center** Faculty Title: **Professor, CMED**
Phone #: **543-1430** FAX #: **685-0305** Box #: **357330**
E-mail: **c/o pattir@bart.rprc.washington.edu**
Co-Investigator(s): Peggy Lalor, Skeletech, Inc.
Samantha Hornby, Skeletech Inc.
Project Title: **Evaluation of an osteoinductive material in nonhuman primate osteopenic vertebrae**
Project Dates: 6/1/00 to 5/31/01 Funding Source(s): commercial contract

Review for Scientific Merit

All animal use projects must be reviewed for scientific merit prior to initiating animal use. The required review for this project (please check one):

☐ ~~has been~~ *will be (review pending)* conducted by my department or school and has been found to be scientifically meritorious (signature of Chairperson or designee required). The review was conducted by:

Primate Center Research Review Committee (name of reviewer(s) or review committee)

William R. Morton, VMD _____
Chairperson Date

☐ will be conducted by a funding agency prior to the start of the project _____ (agency)

☐ has already been conducted and approved by a funding agency _____ (agency)

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: IL CTC: JUN 16 2000

Comments: _____

Initial Reviewer: MP Review Date: 6/12/00

Additional Review Activity and Dates: _____

Date Approved by ACC: JUN 21 2000 (Approval expires one year from this date)

PRF Revised 1998

Principal Investigator Certification Statement

1. I understand that all use of animals or animal tissues must have prior ACC approval. I understand that unauthorized animal use is reportable to the UW Office of Scientific Integrity, the funding agency and the Office for Protection from Research Risks (OPRR). **Therefore, I will obtain approval prior to animal use and prior to instituting any significant changes in the project.** I understand that performance of any animal procedures that have not had ACC approval, by myself or any staff, students, fellows, etc., for whom I am responsible, may constitute Scientific Misconduct.

2. I certify that this Project Review Form accurately describes all aspects of the proposed animal usage and that the proposed work is not unnecessarily duplicative.

3. I accept responsibility for ensuring that all personnel working on this project are aware of, and will not deviate from, the ACC approved procedures outlined on this form, that they will adhere to the regulations regarding the humane treatment of laboratory animals and that they will receive proper training as required by the ACC.

4. I understand that if I (or the contact person listed on this form) cannot be contacted and animals on this project show evidence of illness or pain, emergency care (please indicate contraindicated drugs under #26, PRF-11), including euthanasia may be administered at the discretion of veterinary staff.

5. I understand that the approval is not final until I receive notification of such **in writing**, and that the ACC can recommend or require changes to the protocol.

6. I understand that approval of projects is for a maximum of one year from the date of ACC approval and I must apply for a renewal in order to continue the project beyond that period.

Signature of P.I. (no per signatures) _____ Date 5-11-00

Animal Use Personnel Certification Statement

(All animal use personnel must sign prior to submittal of form -
additional personnel can be added later, by submitting a "New Personnel Form")

I certify that I have read this Project Review Form and that I will only perform procedures that have been approved by the ACC. I understand that any significant changes in procedures must be approved by the ACC prior to implementation.

Signature	Signature
_____	_____
_____	_____
_____	_____
_____	_____

Approval is requested for additional nine monkeys for this project:

1) We expect to screen 15 animals prior to this experiment, to select the 12 for assignment; three animals added to the twelve already approved. The monkeys will receive radiograph and DXA scan procedures done, but no other experiment work. The animals not selected for this project will be returned to the Primate Center Colony, with no permanent changes.

2) We need to add six macaques that will serve as controls for this project. These animals will receive radiograph and DXA scan procedures only. There will be no invasive procedures done to these animals, and they will be returned to the Primate Center Colony at the end of this experiment. There will be no permanent biological changes.

Principal Investigator Certification Statement

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2. I certify that this Project Review Form accurately describes all aspects of the proposed animal usage and that the proposed work is not unnecessarily duplicative.

3. I accept responsibility for ensuring that all personnel working on this project are aware of, and will not deviate from, the ACC approved procedures outlined on this form, that they will adhere to the regulations regarding the humane treatment of laboratory animals and that they will receive proper training as required by the ACC.

4. I understand that if I (or the contact person listed on this form) cannot be contacted and animals on this project show evidence of illness or pain, emergency care (please indicate contraindicated drugs under #26, PRF-11), including euthanasia may be administered at the discretion of veterinary staff.

5. I understand that the approval is not final until I receive notification of such **in writing**, and that the ACC can recommend or require changes to the protocol.

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Signature of P.I. (no per signatures) _____ Date _____

Animal Use Personnel Certification Statement

(All animal use personnel must sign prior to submittal of form -
additional personnel can be added later, by submitting a "New Personnel Form")

I certify that I have read this Project Review Form and that I will only perform procedures that have been approved by the ACC. I understand that any significant changes in procedures must be approved by the ACC prior to implementation.

Signature

Kathy Eggert
Debra Hamilton
Judith A. Johnson
Kay Larsen
Scott A Camp

Signature

Ed Novak
Patrick J Ellis
Peggy Smith
Katherine J. Linde

Contact Person (e.g., questions, renewal notices):

William R. Morton, VMD Phone: **543-1430** Box: **357330** E-mail: **c/o pattir@bart.rprc.washington.edu**

Personnel:

NOTE: Every 5 years all personnel must attend the *"General Session"* which provides training on the regulations and guidelines for the use of animals (list latest date below). Special General Sessions/tapes are available for wildlife and fish studies. All personnel must fulfill this requirement prior to being listed on the project. Principal Investigators must have this training before approval of the protocol can occur. Please contact the animal use training coordinator (616-6849) if you need information on obtaining this training.

Please indicate, in the format below, the duties of all personnel who will be involved with animal use procedures and their training and qualifications to perform those procedures. Include the date(s) of UW Animal Use Training Sessions (AUTS) attended and Topic/Species of AUTS. Please use additional pages as needed.

Name: **Judy Johnson** Position: **Research Support Coordinator**
Years of experience with proposed species: **25**
Duties: **Personnel supervision and coordination** General Session (date): **1/25/00**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1998 – Infectious Substances
1998 Working in Non-Human Primate Areas

Name: **Kathy Eiffert** Position: **Veterinarian Technologist** Years of experience with proposed species: **22**
Duties: **Project performance and sample collection** General Session (date): **1994** 6/3/99
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1996 – Primate Seminar
1998 – Bloodborne Pathogen Control

Name: **Pat Delio** Position: **Animal Scientist** Years of experience with proposed species: **6**
Duties: **Project performance and sample collection** General Session (date): **1996**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1996 – Primate Seminar
1996 – Surgery

Name: **Ed Novak** Position: **Veterinary Technician** Years of experience with proposed species: **7**
Duties: **Project performance and sample collection** General Session (date): **1-6-99**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1996 – Bloodborne Pathogen Control.

Name: **Scott Cramp** Position: **Veterinary Technician** Years of experience with proposed species: **15**
Duties: **Project performance and sample collection** General Session (date): **1995**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1998 AAALAS Training Sessions in Animal Husbandry
1998 – Bloodborne Pathogen Control
1997-98 Bone Marrow Aspirations
1997-98 – Blood Donor Draws
1993-94 Baby Save Supervisor.

Name: **Debra Glanister** Position: **Animal Scientist** Years of experience with proposed species: **17**
Duties: **Project performance and sample collection** General Session (date): **7-24-96**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1997 – Bloodborne Pathogen Control
1997 Radiation Safety

Name: **Mike Gough** Position: **Animal Scientist** Years of experience with proposed species: **14**
Duties: **Project performance and sample collection** General Session (date): **7-24-96**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): **NHP**
Other relevant training (i.e., training for proposed procedures):
1998 – Working in Non-Human Primate Areas;
1995 – Radiation Safety;
1998 – Infectious Substances.

Name: **Carol Elliott** Position: **Animal Scientist** Years of experience with proposed species: **15**
Duties: **Project assistance, sample collection**
General Session (date): **4/00**
Other AUTS (date and class, e.g., 3/1/97 mouse lab):
Other relevant training (i.e., training for proposed procedures): **AALAS, registered LAT**

Name: **Katie Hinde** Position: **Laboratory Technician** Years of experience with proposed species: **1**
Duties: **Project assistance, sample collection**
General Session (date): ~~**4/99**~~ 10/14/98
Other AUTS (date and class, e.g., 3/1/97 mouse lab):
Other relevant training (i.e., training for proposed procedures):
Blood-borne Pathogens, 1999

Name: **Peggy Smith** Position: **Animal Scientist** Years of experience with proposed species: **<1**
Duties: **Project assistance, sample collection**
General Session (date): **4/00**
Other AUTS (date and class, e.g., 3/1/97 mouse lab):
Other relevant training (i.e., training for proposed procedures): **BSC Animal Science, CalPoly '78**

Name: **Kay Larsen** Position: **Research Technologist** Years of experience with proposed species: **5**
Duties: **Project assistance, sample collection**
General Session (date): **1996**
Other AUTS (date and class, e.g., 3/1/97 mouse lab): Primate session, 1996
Other relevant training (i.e., training for proposed procedures):

Occupational Health:

Personnel performing research with animals are required, by federal regulations, to participate in the institution's occupational health program. Please call the UW Occupational Health Nurse (548-4848) to discuss the Occupational Health requirements for this project. Make sure to inform the nurse of all species you will use or will come in contact with as a part of your work (e.g., multiple species in field studies), as well as any other potentially relevant information (e.g., use of viruses, human products, etc.).

The Occupational Health requirements for personnel working on this project are (list required immunizations, vaccines, titer monitoring requirements, etc.):

PPE usage training
Serum banking, semi-annually (recommended)
TB testing, semi-annually (recommended)

In the table below, list requested building and room # for animal use/housing location(s).

Species	Housing (>24 hrs.)	Surgery	Procedures
Macaca nemestrina ***OR*** *Macaca fascicularis*	*Primate Center, HSB I-wing, RR-wing*	*Primate Center surgery suites, HSB I-wing*	*Procedure rooms adjacent to housing rooms, HSB I-wing, RR-wing*

Indicate the planned number of animals for the next year (complete relevant tables).

a. **New**: animals to be purchased in the next year:

Species	Strains	Sex	Ages	Size	Number
Macaca nemestrina ***OR*** *Macaca fascicularis*		*F*	*Aged (>10y)*		*12* ✓

b. **Breeding**: Anticipated number of animals to be born in the next year, as a part of this protocol:

Species	Strains	Number
N/A		

c. **Transfers**: Animals to be acquired from another approved protocol in the next year:

Protocol #	Species	Strains	Sex	Ages	Size	Number
N/A						

d. **Capture**: Anticipated number of animals to be captured in the next year, as a part of this protocol:

Species	Ages	Size	Number
N/A			

e. **Carry-over**: Animals you currently have in house, to be continued on this project into next year:

Species	Strains	Sex	Ages	Size	Number
N/A					

Animal Order/Purchase By: ☐ Comparative Medicine ☒ Primate Center

Veterinary Care By: ☐ Comparative Medicine ☒ Primate Center ☐ Other (specify)_____

NOTE: There are new Federal policies regarding documentation that reduction, replacement, and refinement (the three R's) have been addressed. For all studies in which animals may experience more than momentary pain or discomfort (i.e., greater than that associated with a needle stick) a literature search (or other documentation) is required to determine that less painful/distressful alternatives to your proposed animal use and procedures are not available or feasible. Please note that procedures such as trapping/capturing or procedures requiring the use of anesthetics (including terminal surgeries) have been defined as having the potential for greater than momentary pain or discomfort.

Was a literature search performed? ☒ Yes ☐ No

If "Yes", you must provide the following information (or the protocol cannot be approved):

Databases/Sources	Date of Search	Years Searched	Key Words or Strategy
Medline	May 00	1990 - present	Osteoporosis, animal models, therapies/therapeutics

If "No", please describe how you determined that alternatives to your use of animals, or that less painful/distressful procedures, are not available or feasible.

ASCITES: Recent federal policies require that investigators planning production of monoclonal antibodies by the mouse ascites method, specifically address the reasons that in vitro methods cannot be used.

Describe alternatives to animal use you may employ (or have employed) in this project. Alternatives should reflect refinement, replacement, and reduction of animal use. These include *in vitro* tests, use of less sentient animals, use of fewer animals to attain statistical significance and use of methods to decrease animals' sensitivity to pain.

Studies of osteoporosis in nonhuman primates have consistently demonstrated development of osteopenia accompanied by high bone turnover rates after ovariectomy. These dynamic changes more closely model those occurring in post-menopausal women than other animal model systems.

Describe the rationale for using animals and the appropriateness of species proposed.

Osteopenia in female non-human primates mimics the bone loss seen in osteoporotic human females at risk for vertebral fractures due to structural loss. Also the size of the vertebral bodies in these non-human primates are sufficient to enable injection of the test material.

Provide in detail the method used to determine the number of animals. Inclusion of a Power Analysis is expected, if preliminary data are available for the necessary calculations (use additional pages as needed). For studies where power analysis is not appropriate (e.g., pilot studies, tissue protocols, etc.), provide a brief narrative describing how requested animal numbers were determined.

This experiment will evaluate the effectivenes of an osteoinductive injectable material as a bone densification agent in non-human primate osteopenic vertebrae, a potential therapeutic for osteoporosis.

This study design fits under a standard two-sided Fisher exact test, for comparing two groups when the response is dichotomous, eg only a 'yes/no.' If the response is not dichomotous, or the experimental design is other than two paralle groups, sample size would have to be determined by other means." This leads to two groups of 6 each will allow for (a) study dropouts, and (b) possible therapy 'failures' while retaining sufficient numerical power to determine statistical significance ($p<0.8$).
0.08 per e-mail (RP)

Using language understandable to non-scientists, describe the goals and significance of the project to human/animal health or biology.

See below.

Attach an abstract of the proposed project (a copy of the GC-1 abstract will suffice).

In humans, osteoporosis results in bone loss that puts patients at risk for increased fractures including femoral neck and vertebral body fractures. To increase the mechanical strength of vertebral bodies by increasing bone volume could result in a decrease risk for vertebral fracture. The objective of this study is to evaluate the effectiveness of an osteoinductive injectable material as a bone densification agent in non-human primate osteopenic vertebrae. This material has been shown to promote bone formation in previous studies in other bony sites. Animals will be assessed by methods approved for human clinical evaluation of bone density (DXA) to determine the effect of injection of the material over time. The animals will be evaluated histologically to compare the quality and quantity of bone formation due to injection of the test material.

ANIMAL USE PROCEDURES: Mark the box (either "yes" or "no") for every procedure. If a procedure is marked "yes", answer each part of that question. Make additional space as needed or use additional sheets. If a specific part of that procedure is not applicable to your project, so indicate (e.g., type "NA"). Note: You must provide specific timelines for all procedures, including the endpoint of the study for each animal.

See our website at www.?? for information on ACC policies regarding specific procedures. Adherence to the published policies will facilitate review and approval of procedures.

☐ If public release of this form is requested under the Freedom of Information Act, I wish to have input to ensure that information revealing the experimental hypotheses or design is not released to the public.

 # Yes No

1. [Y] Anesthesia (include pre-anesthetic and anesthetic agents):

a. Provide the information requested in Table form.

Animal Species	Anesthetic Agent	Dose	Route	Procedure (e.g., surgery, blood draws)
Macaca nemestrina OR *Macaca fascicularis*	*Ketamine HCl*	*10-15mg/kg*	*IM*	*Blood draws, other minor procedures*
	Xylazine/Ketamine (each 0.1ml mixture = 7mg ketamine and 0.6mg xylazine)	*0.1 ml/kg*	*IM*	*Minor surgeries*
	Isoflurane inhalation anesthetic	*to effect*	*Via endotracheal tube*	*Experimental injections.*

b. For gas anesthesia, what is the method of scavenging of waste gases (e.g., FAIR canister, fume hood)?

c. What parameters will be monitored to ensure adequate anesthesia (e.g., corneal reflex, heart rate, respiration, etc.).

The surgical suites of the Primate Center have negative ventilation that promotes direct elimination of the waste gases. The surgical support staff of this facility is trained and experienced in the administration of anesthetics, and have monitoring equipment available to assist them: electronic monitoring of HR, respiration, and blood oxygenation, audible alarms and LCD read-outs; monitoring of blood pressure, temperature.

2. [N] Ether use (not recommended)

a. Scientific justification for use of ether (required)
b. Fume evacuation method
c. Most recent certification date of fume hood
d. Room where ether will be used
e. Storage method and location

3. [N] Paralytic agents (anesthesia required)

a. Agent

b. Dose
c. Route of administration
d. Monitoring protocol to ensure adequate anesthesia

4. [Y] **Administration of drugs/reagents/cells/etc. (Answer all parts for each agent and animal species. For antibody or ascites production, answer under # 6 and/or 7 below):**
   a. Agent
   b. Dose/amount
   c. Route of administration
   d. Frequency of administration
   e. Anticipated side effects
   f. Monitoring protocol

This experiment will evaluate the effectivenes of an osteoinductive injectable material as a bone densification agent in non-human primate osteopenic vertebrae. This product is currently under clinical investigation in Europe and the US for treatment of distal radius and tibial fractures. Over 150 patients have been treated to date with no reports of adverse reactions or other concerns.

A series of biocompatibility tests on this formulation have been conducted in accordance with FDA GLP regulations. The purpose of this series of tests was to determine the presence of toxic or irritant components. These test are also in accordance with ISO requirements (harmonized biocompatility requirements) and were performed by NamSA (Northwood, Ohio and Irvine, California). This table summarizes the results of those tests:

Study	Species	Result
Muscle implantation 1, 4, 13 weeks [0.2ml/site, 6 sites, total of 0.5ml/kg]	*Rabbit*	*No macroscopic reaction, slight irritant at one week, non-irritant at 4 and 13 weeks*
Genotoxicity, sister chromatid exchange	*In vitro*	*Not genotoxic*
Genotoxicity, chromosomal aberration	*In vitro*	*Not genotoxic*
Genotoxicity, Ames test, saline	*In vitro*	*Not mutagenic*
Pyrogenicity, rabbit pyrogen study [0.14 ml/kg]	*Rabbit*	*Nonpyrogenic*
Acute systemic IV toxicity [0.57 ml/kg]	*Mouse*	*No mortality or evidence of systemic toxicity*
Acute intracutaneous reactivity [0.2 ml extract/site, 5 sites, total of 0.4 ml/kg]	*Rabbit*	*Evidence of very slight to moderate erythema and edema*
Delayed contact sensitization [0.1 ml extract/site, 2 sites, total of 0.6ml extract/kg	*Guinea pig*	*No delayed dermal contact sensitization*
Hemolysis [1:6 dilution]	*In vitro*	*Inconclusive results due to viscosity of test solution. Revise and repeat test.*
Hemolysis, repeat [1:100 dilution]	*In vitro*	*Non-hemolytic, mean hemolytic index of 1%*
Cytotoxicity [1:6 dilution]	*In vitro*	*False positive result due to precipitation of formulation in tissue culture medium at 37°C. Revise and repeat test.*
Cytoxicity, repeat [1:100 dilution]	*In vitro*	*No evidence of cell lysis or toxicity*

The test material and control material will be injected directly into the vertebral body of the lumbar vertebrae L3 and L5. The site will be accessed surgically (ref. Q 15 below). The volume to be injected will be determined by the capacity of the vertebral body in each individual animal, as determined by DXA scan and radiography (also ref Q15). All animals will be given post-operative analgesics following surgery. Animals will be monitored daily for general activity, appetite, and stool consistency. At the time of the monthly radiographic and DXA procedures, blood will be collected for CBC and serum chemistry panel. Any abnormalites noted, in the animals' daily activity or in the blood work, will be reported to the Clinical Veterinarian of the Primate Center, who will evaluate the animal for clinical treatment.

5. [N] **Toxicity testing**

a. Protocol
b. Side effects expected
c. Monitoring protocol
d. Endpoint: ☐ Euthanasia ☐ Spontaneous Death ☐ Other (explain)

6. [N] **Antibody production (for ascites production, skip to #7 below)**

a. If antibody production service will be provided by the Comparative Medicine Antibody Resource Laboratory, indicate that and specify the immunizing agent. If all procedures will conducted by your own research staff, provide all of the information requested in the table below.

	Immunizing Agent (antigen)	Adjuvant	Number and Site(s) (IP, IM, SQ, etc.) of inoculation	Volume per inoculation site
Primary Immunization				
Booster Immunization				

7. [N] **Ascites Production**

a. Species (e.g., mice)
b. Priming agent (e.g., Pristane)
c. Injection volume (for mice, not to exceed 0.2ml for Pristane)
d. Route of administration
e. Hybridoma cell injection protocol (e.g., dose, # days after priming)
f. Monitoring protocol (minimum required following initial inoculation: 3 times/week the first week and daily thereafter)
g. Ascites collection protocol, including number of taps, needle size, etc. (note: euthanasia required after 2nd tap, unless scientifically justified)

8. [N] **Tumor transplantation/ induction or spontaneous growth**

a. Type
b. Site
c. Functional deficits expected
d. Monitoring protocol (at least 3 times per week required)
e. Provide assurance that animals will be euthanized before tumors exceed 10% of normal body weight or provide scientific justification for larger tumors

9. [N] **Potentially hazardous agents (answer all parts for each agent)**

a. Has approval been obtained from the appropriate Environmental Health and Safety Committee (e.g., Recombinant DNA, Biohazards, Chemical, Radiation Safety, etc.)?
- Note: your protocol cannot be approved by the ACC prior to EH&S approval

b. For Comparative Medicine housing, indicate that a copy of the protocol has been provided to the Facility Manager, Gary Millen (543-0641, Box 357190)

c. Indicate any special housing requirements

d. Dose(s) of agents to be used

e. Effects on animals

f. Monitoring protocol

g. Danger to humans

h. Precautions to protect personnel

i. Special containment requirements

j. Special disposal requirements for agents and animals

10. [Y] **Blood Sampling (answer for each animal species)**

a. Species

b. Method

c. Site

d. Volume (describe monitoring/replacement therapy if greater than 10ml/kg in a 2 week period)

e. Frequency

The only blood collections planned are intended to provide clinical monitoring of the animals. At monthly intervals (minimum), blood will be collected for CBC and serum chemistries. The volume required for this would be less than 15 ml at each bleed.

11. [Y] **Imaging procedures (radiographs, ultrasounds, MRI, etc.)**

a. Type of procedure
Dual-energy x-ray absorptiometry (DXA) and radiographic procedures will be required to screen all candidate macaques for this experiment, to determine the degree of existing osteoporosis in the vertebral bodies.

b. Frequency
The macaques will have an initial imaging session to determine the appropriateness for assignment. After injection of the test material, the DXA scan and conventional radiology will be repeated monthly for six months, to evaluate bone formation and changes in density.

c. Purpose (e.g., imaging only, tumor treatment, etc.)
The first DXA scan will be to screen potential candidate macaques for assignment to the experiment. Subsequent DXA and radiology procedures will be to monitor changes in bone density and bone formation following the experimental procedure.

d. Effects on animals
These are standard imaging procedures with no adverse effects to the macaques.

12. [N] **Use of restraint (not applicable for brief restraint such as holding for blood sampling)**
   a. Species
   b. Method
   c. Frequency
   d. Duration of restraint
   e. Scientific justification for prolonged or painful restraint

13. [N] **Implanted catheters, prostheses, etc. (describe applicable surgery under # 15)**
   a Type
   b. Site
   c. Monitoring protocol for animal health
   d. Maintenance and care of chronic implants

14. [N] **Terminal surgery (i.e., no recovery from anesthesia)**
   a. Describe surgical procedure
   b. Duration of procedure

15. [Y] **Survival surgery**
   a. Number of surgeries per each animal
   One

   b. Describe surgical procedure(s)
   The animal will be placed in ventral recumbancy; the entire lower back will be shaved and prepped for surgery, ie scrubbed with a disinfectant soap (eg Betadine) and draped with sterile towels and drapes. The dorsal and lateral processes of the lumbar vertebrae L3, L4, and L5 will be identified and marked. The experimental substance will be injected directly into the vertebral body of L3 and L5 percutaneously. The volume to be injected and the depth of the injections will be determined from currently ongoing studies with tissues recovered from macaques through the Primate Center's Tissue Program. This information, combined with the each individuals' capacity as estimated from the DXA scans and radiographs, will determine the final volume to be injected into each animal.

   c. Pre-operative protocol (e.g., food/water restriction, animal prep.)
   Animals are not fed the evening prior to a surgical procedure, which will result in a food restriction period of at least 12 hours. Water is not restricted. Pre-operative antibiotics will be prescribed and administered by the Clinical Veterinary staff of the Primate Center. The animal will be placed in ventral recumbancy; the entire lower back will be clipped and shaved to be free of hair and then prepped for surgery, ie scrubbed with a disinfectant soap (eg Betadine) and draped with sterile towels and drapes.

   d. Aseptic precautions (must include method of instrument sterilization prior to initial use and between animals, if applicable)
   All materials used in surgical procedures are sterilized by standard hospital techniques (steam autoclave or gas sterilization), or are disposable supplies provided in pre-sterilized packaging from the manufacuterer. Sterilization is confirmed by commercial indicators that show color change or other visible read-outs.

e. Supportive care during procedure (e.g., IV fluids if needed)
This is a relatively non-invasive procedure, no opening or penetration of a body cavity, and supportive fluid therapy is not required. Anesthetized animals are provided with external heat to prevent hypothermia. All animals are fully monitored during the anesthetic procedure to ensure that heart rate, blood pressure, and body temperature stay within safe limits.

f. Duration of procedure
One to 1½ hours

g. Post-surgical monitoring protocol including number of days monitored by research staff
Animals will be monitored after surgery to ensure full recovery from anesthetic. After the animals are returned to their home cages, observation will continue for signs such as loss of appetite, reluctance to move or any other adverse signs. Post-operative analgesics will be prescribed and administered by the veterinary staff as described in Q16 for the minimal period of 48 hours. This may be extended at the discretion of the Clinical Veterinarian.

h. Time point for suture/staple/clip removal (explanation required, if greater than 14 days)
N/A

i. Deficits expected as a result of the surgery
None

j. For multiple major survival surgeries on a single animal provide (1) scientific justification and (2) length of time between surgeries. (Major surgery is defined as one that penetrates and exposes a body cavity or which produces a permanent impairment of physical or physiological functioning.)
N/A

16. [Y] **Potentially painful procedure - applicable for all procedures that would be considered painful in the absence of anesthesia or analgesia (e.g., terminal or survival surgery, etc.)**
a. Pain assessment protocol (i.e., what is monitored, how is it monitored and how often?)
b. Planned analgesic(s)
c. Analgesic dose
d. Route of administration
e. Frequency of administration
f. Scientific justification if analgesics are to be withheld from animals with signs of pain

All surgical procedures are assumed to cause pain and/or discomfort. Analgesics are provided as prescribed by the Clinical Veterinary staff for at least the first 24 – 48 hours post-operatively, with Tylenol orally subsequent to that. Administration of analgesics may be extended at the discretion of the clinical veterinarian, based on clinical signs. Among the analgesics in use at the Primate Center are:

Ketofen IM, 5mg/kg BID
Butorphanol IM, 0.15mg/kg BID
Buprenex IM, 0.1-0.3 mg/kg BID/TID

17. [N] **Capture/Trapping (Note: obtaining required permits is the responsibility of the PI and is required prior to start of project)**
   a. Protocol
   b. Duration animals will be in traps or restrained
   c. Indicate non-target species that may be inadvertently captured
   d. Disposition of animals (e.g., euthanized, released, etc.)

18. [N] **Special diet (e.g., high fat, etc.)**
   a. Composition of diet
   b. Amount
   c. Duration
   d. Anticipated side effects (e.g., anticipated % weight loss or gain, dehydration, etc.)

19. [N] **Food/Water restriction of 12 hours or more**
   a. Indicate what is restricted and duration
   b. Anticipated side effects (e.g., anticipated % weight loss, dehydration, etc.)
   c. What parameters will be monitored, and how often will animals be monitored for health and well-being
   d. Scientific justification for restriction
   e. Scientific justification for weight losses greater than 20% of baseline (or controls)

20. [N] **Behavioral testing:**
   a. Describe testing procedures (including stimuli and restraint)
   b. Scientific justification for use of noxious stimuli

21. [N] **Transgenic or Knockout animal use or production**
   a. Method of production (e.g., embryo transfer, superovulation procedures, breeding, etc.)
   b. Method/protocol for genetic verification (e.g., age, amount of tissue, use of anesthetics, etc.)
   c. Anticipated effects of genetic manipulation (e.g., spontaneous death, tumors, etc.)
   d. Method and frequency of monitoring health and well-being
   e. Disposition of non-transgenics (e.g., use as controls, euthanasia, etc.)

22. [N] **Breeding colony that will supply other protocols or research projects**
   a. Breeding method (e.g., pair, harem)
   b. Protocol (e.g., randomizing procedures, breeder culling criteria, etc.)
   c. For inbred, specify # of generations from source
   d. For outbred stocks, specify method to ensure lack of inbreeding
   e. Any other quality control procedures
   f. For inbred strains, provide a description of record systems and documentation of animal pedigrees, production and disposition

23. [N] **Will some animals live out their normal life spans as a part of this project?**
   a. Indicate usage of these animals (e.g., breeders, blood donors, experimental animals)

24. [N] **Spontaneous death of animal, instead of euthanasia (e.g., toxicity studies, LD50 studies, etc.)**
   a. Written scientific justification (required), including the reason(s) euthanasia is not possible
   b. Monitoring protocol

25. [Y] **Non-physical Euthanasia and physical euthanasia on <u>anesthetized</u> animals (answer for each animal species)**
   a. Agent (drug, dose, route) for non-physical method
   b. Physical method for anesthetized animals
   c. Criteria used to decide upon euthanasia (e.g., illness, tissue harvest, end of study, etc.)
   d. Scientific justification for methods not approved by the AVMA Panel on Euthanasia (JAVMA 202:229-249, 1993)

All animals will be euthanatized at the end of the experiment by the administration of an overdose of sodium pentobarbital, intravenously, under ketamine sedation. The decision on whether or not to perform this procedure earlier than required by experimental protocol will be based strictly on clinical evaluation of the animal. In this regard, we will use the same criteria we presently use for all projects at the Primate Center and which is described in detail in the RPRC S.O.P. Manual - i.e., if a disease condition develops that cannot be alleviated or treated to prevent chronic pain or suffering, the animal is euthanized.

26. [N] **Physical Euthanasia <u>without anesthesia</u> (answer for each animal species)**
   a. Method
   b. As per AVMA Panel on Euthanasia recommendation, scientific justification is required
   c. Personnel performing procedures must be certified by Comparative Medicine Veterinary Staff (personnel can be certified during AUT labs or arrange with Veterinary Services)
      1. List personnel
      2. Date of certification
      3. Name of veterinary staff member who provided certification
   d. Criteria used to decide upon euthanasia (e.g., illness, tissue harvest, end of study, etc.)

27. [Y] **Collection of tissues**
   a. Time point for collection
   b. Tissue(s) to be collected

At the time of euthanasia, necropsy will be performed. A full gross evaluation will be made of all organs and systems. The lumbar vertebrae 3, 4, and 5 will be removed from detailed histologic examination. Tissue samples from heart, liver, lungs, kidneys, spleen, and regional lymph nodes will also be collected for detailed histologic examination.

28. [N] **Other procedures not listed elsewhere (describe)**

29. [N] **Are there any medications or procedures which should not be administered by veterinary personnel because they would render the results of the study invalid. Please list them.**

30. [Y] **If this study involves the use of non-human primates, will they be involved in an environmental enrichment program? If not, written scientific justification is required.**

Morton 2409-68

Date: Mon, 5 Jun 2000 15:54:18 -0700 (PDT)
From: Nona Phillips <nonap@u.washington.edu>
To: pattir@bart.rprc.washington.edu
Cc: aschmidt@bart.rprc.washington.edu
Subject: Bill Morton's new protocol 2409-68 "Evaluation of an Osteoinductive Material in Nonhuman Primate Osteopenic Vertebrae"

Patty and Ann,

I've just finished my review of Bill's new protocol. There are just a couple of items that we need taken care of:

6/12/00 NP

1. Scott Cramp needs to update his General Session "Laws and Regulations" training. I believe you all have a copy of the video so he can just watch it and then please let us know the date.

2. Carol Elliott didn't sign the form so you could send us a signed copy of the signature page or she can send me an e-mail agreeing to the following statement:

"I certify that I have read the Project Review Form and that I will only perform procedures that have been approved by the ACC. I understand that any significant changes in procedures must be approved by the ACC prior to implementation."

3. I believe there's a typo in the second paragraph explaining the rationale for the number of animals requested. It states "...to determine statistical significance ($p<0.8$). I believe that you intended to say the Power would equal approximately 0.8 (or 80%) with $p<0.05$. Could you confirm that please?

Thanks!

Nona

Nona Phillips, Ph.D.
IACUC Executive Secretary
Department of Comparative Medicine
Box 357190
phone: (206) 543-3818
FAX: (206) 685-3006

From: "Carol Elliot" <carole@bart.rprc.washington.edu>
Organization: Primate Center U of W
To: nonap@u.washington.edu
Date: Tue, 13 Jun 2000 07:22:38 pst -800
Subject: 2408-68
CC: ASCHMIDT@bart.rprc.washington.edu
Priority: normal
X-mailer: Pegasus Mail for Windows (v2.50)

Nona,
I realized this morning that I did not give you the ACC number of the protocol I recently read, so here is another e-mail including the ACC number.

"I certify that I have read the Project Review Form for ACC number 2409-68 and that I will only perform procedures that have been approved by the ACC. I understand that any significant changes in procedures must be approved by the ACC prior to implementation."

Carole

Date: Wed, 07 Jun 2000 14:29:21 -0700
From: Ann Schmidt <aschmidt@bart.rprc.washington.edu>
To: nonap@u.washington.edu
Subject: Fwd: Re: protocol 2409-68 Evaluation of an Osteoinductive Material....

" I believe there's a typo in the second paragraph explaining the rationale for the number of animals requested. It states "...to determine statistical significance ($p<0.8$). I believe that you intended to say the Power would equal approximately 0.8 (or 80%) with $p<0.05$. Could you confirm that please?"

Nona, this is my typo error. Should have said "p = or < 0.080" (lost track of my decimal place.)

Ann Schmidt
University of Washington
Regional Primate Center
HSB Box 357331
Seattle, WA 98195-7331
(206) 616-9202
fax (206) 221-2820

University of Washington

R 5 1998 Project ID#: 2187 - 16

Animal Care Committee
Significant Change Form

ANIMAL CARE COMMITTEE

Request for Significant Change of Animal Use Protocol

Please type-handwritten forms will be returned

Principal Investigator/Project Director: Gene P. Sackett
Department: Regional Primate Research Center Faculty Title: Core Staff
Project Title: Acute and Chronic Effects of Prenatal Tethering and Psychological Stress
Project Dates: _____ to _____ Funding Source(s): NIH

☒ Request for approval of significant change in animal use or protocol. Provide a detailed description of methods and procedures. A list of significant changes is available in the Department of Comparative Medicine Information Manual. This list is by no means exhaustive, but is meant to illustrate the type of changes which require Animal care Committee approval. Requests for the Information Manual or information on significant changes may be directed to the ACC Coordinator, 543-3818. If this request involves an increase in the number of animals to be used during the current year, state the number and species requested and provide the method used to determine the number of animals. **(This will not change the annual renewal date of your project.)**

We propose the administration of two antibiotic drugs, Gentamicin and Pipracillin, be given to the chronically-catheterized animals on this project towards the end of their pregnancies. It has been shown by other investigators using this animal model that there is an increased success rate of fetal/infant viability when these drugs are administered 10-14 days before anticipated delivery of the infants. With the advice of Cathy Johnson-Delaney, Clinical Veterinarian for the Primate Center, we propose a dose of piperacillin at 100-150 mg/kg BID IV and a dose of gentamicin at 2-3 mg/kg BID IV (diluted in saline and delivered slowly over 20-30 min).

Certification Statement

I certify that the attached Project Review form accurately describes all aspects of the proposed animal usage. I further certify that the use is not unnecessarily duplicative. I accept responsibility that all personnel working on the project will adhere to the regulations regarding the humane treatment of laboratory animals and will receive proper training as required by the ACC. I will obtain approval prior to instituting any significant changes in the project. I understand that the approval is not final until I receive notification of such in writing, and that the ACC can require changes to the protocol. I understand that approval of projects is for a maximum of one year **from the date of ACC approval** and will apply for a renewal.

James Sackett For Gene P. Sackett — 3 Mar 98
(Signature of P.I.) (Date)

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: II CTC MAR 19 1998
Comments: _____ Initial Reviewer: MP
Review Date: 3/10/98 Interim Approval Date: 3/10/98
Significant Change Approval Date: _____ Date Approved by ACC: APR 08 1998
(Approval expires one year from this date) PRF Revised 3/96

Comments: _____ Initial Reviewer:
_____ Review Date: _____ Interim Approval Date: _____ Date Approved by ACC: _____
_____ (Approval expires one year from this date) PRF Revised 3/96

University of Washington
Animal Care Committee
Significant Change Form

Project ID#: 2187 -- 16

ANIMAL CARE COMMITTEE

Request for Significant Change of Animal Use Protocol

Please type-handwritten forms will be returned

Principal Investigator/Project Director: Gene P. Sackett
Department: Primate Center Faculty Title: Professor
Project Title: Acute and Chronic Effects of Prenatal Tethering and Catheterization
Project Dates: 11/97 to 3/01 Funding Source(s): Primate Center Core: Basic Sackett

X Request for approval of significant change in animal use or protocol. Provide a detailed description of methods and procedures. A list of significant changes is available in the Department of Comparative Medicine Information Manual. This list is by no means exhaustive, but is meant to illustrate the type of changes which require Animal care Committee approval. Requests for the Information Manual or information on significant changes may be directed to the ACC Coordinator, 543-3818. If this request involves an increase in the number of animals to be used during the current year, state the number and species requested and provide the method used to determine the number of animals. **(This will not change the annual renewal date of your project.)**

Certification Statement

I certify that the attached Project Review form accurately describes all aspects of the proposed animal usage. I further certify that the use is not unnecessarily duplicative. I accept responsibility that all personnel working on the project will adhere to the regulations regarding the humane treatment of laboratory animals and will receive proper training as required by the ACC. I will obtain approval prior to instituting any significant changes in the project. I understand that the approval is not final until I receive notification of such in writing, and that the ACC can require changes to the protocol. I understand that approval of projects is for a maximum of one year **from the date of ACC approval** and will apply for a renewal.

James C Ha for GPS 10 Feb 98
(Signature of P.I.) (Date)

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: II CTC MAR 0 4 1998
Comments: _____ Initial Reviewer: _____
NP Review Date: 2/10/98 Interim Approval Date: 2/10/98
_____ Significant Change Approval Date: APR 08 1998 Date Approved by ACC: _____
_____ (Approval expires one year from this date) PRF Revised 3/96

Nona Phillips
Animal Care Committee
Comparative Medicine
University of Washington

in re: SIGNIFICANT CHANGE TO ACUTE AND CHRONIC EFFECTS OF PRENATAL TETHERING AND CATHETERIZATION PROTOCOL

Nona:

The surgeons on our project, Cliff Astley and John Weyhrich would like to practice catheterization of small blood vessels prior to surgery. Surgeries of this type are relatively rare, 4 - 5 months apart, and they feel practicing on rats enhance the success of the 12 fetal surgeries upcoming on the approved project. Therefore, we are requesting a significant change of animal use protocol in order to add a new species to our current protocol. We will require two rats prior to each surgery on which the surgeons can perform catheterization (2 rats X 12 surgeries = 24 rats).

Procedure:

One or two days prior to each surgery, two Long Evans rats (N = 24) obtained from Guthrie Hall (via Bryan Johnson) will be transported to the Primate Center Surgical Suite. John Weyhrich will anesthetize the rats with a combination of Ketamine (10mg/kg) and Xylazine (3 mg/kg), administered intraperitoneally, and monitor anesthetic depth throughout the procedure. Minimally invasive cut-downs over the rats' cervical regions will allow access to the carotid artery and jugular vein. Catheters will be placed in these vessels using the technique employed in fetal macaque catheterization. At the conclusion of the procedure, Joh Weyhrich will perform euthanasia which will be attained with an intraperitoneal or intracardiac injection of sodium pentobarbital.

Thankyou,

Matthew Novak

December 30, 1997
Regional Primate Research Center
Box 357330
University of Washington
Seattle, Washington 98195

JAN - 1 1997

Tena Smith
Animal Care Committee, Coordinator
Box 357190
University of Washington
Seattle, Washington 98195

Re: Procedure to be added to ACC Protocol # 2187-16 "Acute and Chronic Effects of Prenatal Thethering with Catheterization"

Tena,

We would like to add the following procedure to our protocol. It will not require any additional anesthetization of the animals, and takes only a minute or two. This will produce only a minimal of additional handling.

Vaginal Swab Collection in Pregnant Macaques:

Vaginal swabs will be collected when the animals are sedated for ultrasounds. At each timepoint, the animal will be fully sedated. After completion of the ultrasound, the perineal area will be cleaned using gauze pads, dry or moistened with saline, and a sterile speculum will be inserted into the vagina. A sterile dacron swab will be used to gently swab the anterior 2/3 of the vagina avoiding the cervix. Swabbing will be repeated with a new swab, for a total of two swabs/collection. The swab will then be placed into a sterile vial of medium and immediately frozen in dry ice, and then placed into a -70°C freezer.

This procedure is utilized for collection of vaginal secretions in women during pregnancy with no adverse effects.

We would like to start this procedure next week, if we can get verbal approval. I am out of town, so the contact person for approval or more information is Matthew Novak (3-1440) who is coordinating the project for me. Please let us know if there is any further information that I can provide for you about this addition. Thankyou.

Sincerely,

Jim Sackett/jch

II CTC JAN 16 1998

Jim Sackett

Approved FEB 05 1998

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

Gene P. Sackett, Ph.D.
Regional Primate Research Center
E-mail: jsackett@bart.rprc.washington.edu

I-421 Health Sciences Center, Box 357330
Telephone: (206) 543-0440
Fax: (206) 685-0305

November 21, 1997

UW ACUC Committee
% Tena Smith
Box 357190

Dear Tena:

The Primate Center asked me to update the personnel list for our tethering-stress study (ACC Protocol 2187-16). I am sending you the personnel page from the RPRC Project Authorization form. It inclused the original personnel plus others that have joined the project recently. If you need more information or a different format for this information please let me know.

Very Truly Yours,
Gene P. Sackett

Gene P. Sackett
Professor, Psychology
Core Staff, Primate Center

CC Steve Meyer

CTC JAN 16 1998

T Smith 12.1-97

Regional Primate Research Center
University of Washington
(UW RPRC)

Project Number -
(will be assigned by RPRC)

RESEARCH PROJECT AUTHORIZATION REQUEST

Principal Investigator/Project Director: Gene P. Sackett

Project Title: Acute and Chronic Effects of Prenatal Tethering and Catheterization

Date of Request: 11/1/97 Funding Source: Basic Sackett

Academic and Technical Personnel Involved In Project:

Are all animal use personnel enrolled in the UW/RPRC Occupational Health Program? X YES ❑ NO

Name	Title	Duties	Phone # (office,pager)
Gene P. Sackett ✓	Professor	Research design and analysis	543-2500
James Ha ✓	Research Assistant Professor	Computer systems, research design	543-2420
Connie Nosbisch ✓	Research Technician	Maintaining tethering system; blood, fecal, amniotic fluid, and urine sampling;	616-7401
Matthew Novak ✓	Research Assistant	Coordinating project; maintaining tethering system, behavioral and physiological data collection	543-1440
Sam Wasser ✓	Assistant Professor	fecal and urine hormone assays	543-0670
Larry Shields ✓	Assistant Professor	Ultrasound	543-3714
Sue Conrad ✓		Ultrasound	
Gerry Ruppenthal ✓	Research Scientist	Coordinating project Timed Mating	543-3707
Coleen Walker-Gelatt ✓		Supervising postnatal behavioral data collection	543-9169
John Weyhrich ✓	Senior Veterinerian	catheterization surgery	543-3375

University of Washington
Animal Care Committee
Annual Renewal Form

Project ID#: 2 1 8 7 1 6

ANIMAL CARE COMMITTEE

Request for Annual Renewal of Animal Use Protocol

Please type-handwritten forms will be returned

Principal Investigator/Project Director: Gene P. Sackett
Department: Primate Center- Psychology Faculty Title: Professor
Project Title: Acute and Chronic Effects of Prenatal Tethering (delete "Psychological Stress"
Project Dates: 5/1/97 to 5/31/2001 Funding Source(s): RR00166

☐ I am requesting annual renewal of this animal use protocol. (Please provide all information requested below.)

Animals to be used in the following year					
Species	**Strains**	**Sex**	**Ages**	**Size**	**Number**
M. nemestrina		Female	Adult		8
M. nemestrina		F & M	Newborn		8 16

☞ Provide in detail the method used to determine the number of animals. The approved protocol calls for 12 tethered and 12 controls, 6 male and 6 female offspring in each group. This sample size is needed to attain sufficient statistical power, given that prior research has revealed sizeable sex differences in prenatal stress effects in rats, monkeys, and humans.

☞ What is the current status of this project? Have any problems been encountered regarding the animal usage in this project? This project will start in Dec., 1997. It has been held up by decisions concerning remodeling of the 1st floor RR-Wing IPRL space and situating the RPRC Seattle breeding colony. So, other than a late start, no problems have been encountered.

Certification Statement

I certify that the attached Project Review form accurately describes all aspects of the proposed animal usage. I further certify that the use is not unnecessarily duplicative. I accept responsibility that all personnel working on the project will adhere to the regulations regarding the humane treatment of laboratory animals and will receive proper training as required by the ACC. I will obtain approval prior to instituting any significant changes in the project. I understand that the approval is not final until I receive notification of such in writing, and that the ACC can require changes to the protocol. I understand that approval of projects is for a maximum of one year **from the date of ACC approval** and will apply for a renewal.

Gene Sackett
(Signature of P.I.)

11/17/97
(Date)

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: II

CTC DEC 1 1997

T Smith 11.19.97

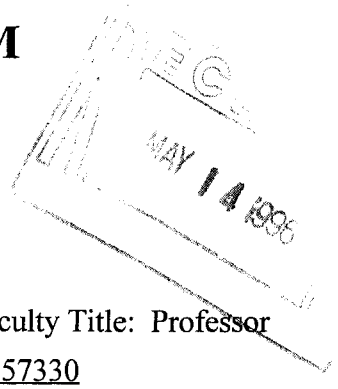
Approved DEC 31 1997

University of Washington
Animal Care Committee

Project ID#: 2118171 116

PRF-1

ANIMAL CARE COMMITTEE
PROJECT REVIEW FORM
For new projects or three-year renewals



Please type -- handwritten forms will be returned

This Project Review Form is available on computer disk

Principal Investigator/Project Director: Gene P. Sackett

Department: Psychology- Primate Center Faculty Title: Professor

Phone #: 543-2500 FAX #: 685-8606 Box # 357330

E-mail: jsackett@bart.rprc.washington.edu

Co-Investigator(s): James C. Ha

Project Title: ACUTE AND CHRONIC EFFECTS OF PRENATAL TETHERING AND PSYCHOLOGICAL STRESS

Project Dates: May, 1997 to April 30, 2000 Funding Source: NIH-NCRR

Certification Statement

I certify that the attached Project Review form accurately describes all aspects of the proposed animal usage. I further certify that the use is not unnecessarily duplicative. I accept responsibility that all personnel working on the project will adhere to the regulations regarding the humane treatment of laboratory animals and will receive proper training as required by the ACC. I will obtain approval prior to instituting any significant changes in the project. I understand that the approval is not final until I receive notification of such in writing, and that the ACC can require changes to the protocol. I understand that approval of projects is for a maximum of one year **from the date of ACC approval** and will apply for a renewal.

Gene P. Sackett May 7, 1997
(Signature of P.I.) (Date)

Review for Scientific Merit

All animal use projects must be reviewed for scientific merit prior to initiating animal use. The required review for this project (check one):

☒ Will be conducted by a federal funding agency prior to the start of the project

☐ Has been conducted by my department or school and the project has been found to be scientifically meritorious (***signature of Chairperson or designee required)

(***Signature of Department Chair) (Date)

(ANIMAL CARE COMMITTEE USE ONLY - DO NOT WRITE BELOW THIS LINE)

Animal Use Categorization: H CTC JUN 0 3 1996

Comments:

Initial Reviewer:

Review Date: 5/16/96 Interim Approval Date: Additional Review Activity and Dates:

Date Approved by ACC: JAN 3 1 1997

(Approval expires one year from this date) PRF Revised 3/96

University of Washington
Animal Care Committee

PRF-2

For additional technical information call:

James C. Ha (Name) Phone: 543-2420
E-mail: jcha@u.washington.edu

Please indicate the duties of all personnel who will be involved with animal use procedures and their training and qualifications to perform those procedures. Please indicate (A) Years of experience with proposed species; (B) Date(s) of UW Animal Use Training Sessions (AUTS) attended; (C) Topic/Species of AUTS; and (D) Other formal animal use training. Continue on another page if necessary.

Name	Position	Duties	A	B	C	D
Gene Sackett	Professor-PI	Overall Scientific Management	33	1995	Pri-mates	
James Ha	Scientist	Data Management	6	1995	Pri-mates	
WaRPRC Colony Personnel	Veterinarian Vet Techs					

Are all animal use personnel enrolled in the UW Occupational Health Program ☐ YES ☐ NO

Location where animals will be housed for 24 hours or more: RR Wing- Infant Primate Research Lab
(room and building)

Location(s) where animal use procedures will be performed:Infant Primate Research Lab

Lab Room # Not yet determined Surgery Room # Primate Center

Animals to be used in the following year					
Species	**Strains**	**Sex**	**Ages**	**Size**	**Number**
M. nemestrina		Fem	Adult		12
M. nemestrina		Both	Fetus-Infant		6

Animal Purchase By: ☐ Comparative Medicine ☐ Other (specify) Primate Center

Veterinary Care Provided By: ☐ Comparative Medicine ☐ Primate Center
☐ Other (specify) _____

University of Washington
Animal Care Committee

PRF-3

☞ **For all studies in which animals may experience more than momentary pain or discomfort, a literature search is required to determine that adequate alternatives to your proposed animal use are not available or feasible.**

Was a literature search using the keywords "Alternatives" or "Animal Testing Alternatives performed?

☐ Yes ☐ No

Please describe how your literature search was conducted and the database(s) you used.

If no, please describe how you determined that alternatives to your use of animals are not available or feasible.

This project will study prenatal stress in a macaque monkey species. One form of this will involve tethering so that chronic catheters can be inserted to collect blood and infuse tocylytics to maintain pregnancy-- a procedure in use in the WaRPRC for the past four years. No data are available concerning the effects of tethering and catheterization alone on pregnancy, fetal development, or offspring postnatal development in any primate species. Further, there are no data concerning relationships between acute and chronic effects of prenatal psychological stress for any primate species- including humans. This was determined through a search of MedLine and PsychInfo, as well as the WaRPRC Primate Information Center data base. There are no alternatives except to use live animals to study these prenatal effects on *M. nemestrina* for basic science purposes or for the use of AIDS-related and other prenatal studies employing the tethering technique.

☞ **Describe alternatives to animal use you may employ in this project**. Alternatives reflect the three Rs of animal use; refinement, replacement, and reduction. These include *in vitro* tests, use of less sentient animals, use of fewer animals to attain statistical significance and use of methods to decrease animals' sensitivity to pain.

The total sample size for this study will be 48 animals, in four groups of 12. Each group will contain six females and six males. Based on our previous work in the WaRPRC on fetal development and on postnatal growth and behavior of offspring, this will be a sufficient sample size to detect real differences with statistical power ranging from .60-.90. It is crucial to study both female and male offsrping, as previous work by us and in other laboratories with primate and nonprimate species have shown large sex differences in the effects of prenatal stress on fetal and postnatal development.

☞ **Describe the rationale for using animals and the appropriateness of species proposed.**

Several projects in the past four years at the WaRPRC have involved the use of tethering and catheterization to study AIDS-related viruses, drugs, and vaccines on pregnant pigtail macaques, their fetuses, and postnatal development of their surviving offspring. To date, no work has been done on the effects of tethering and catheterization alone, procedures that are potential physiological and psychological stressors. Further, no work has been done to determine whether the tether-catheter system interacts with other prenatal psychological stressors such as periodic capture or the loud or surprising stimulation that frequently occurs in the BSL-3 environment. This project will gather the necessary data for validating the degree of stressfulness of these procedures, and will allow other investigators to address the issue that tether-catheter alone-- not the virus, drug or vaccine-- has produced the effects found in their studies.

☞ **Provide in detail the method used to determine the number of animals.**

see section on Alternatives to Animals above.

☞ **Using language understandable to non-scientists, describe the goals and significance of the project to human/animal health or biology.**

HUMANS

Psychological stress and anxiety during pregnancy is considered by many to be a major factor in causing fetal loss, prematurity, low birth weight, and a variety of postnatal deficits in learning, emotion, and social behavior. However, to date there have been no studies simultaneously measuring the acute responses of the mother and her fetus during repeated periods of stress. This means, of course, that there have been no studies directly measuring the relationship between the effects of repeated acute stress on the chronic problems presumably produced by prenatal stress. Until this relationship is established-- a very difficult if not impossible task for experimental-causal research on humans-- the role of prenatal stress on pregnancy outcome and offspring development will remain theoretical rather than an empirical fact. This research, which will use a noise stressor found previously to have effects on pregnancy outcome and offspring development in rhesus macaques, will provide the first experimental data on a primate species concerning the relationship between acute and chronic effects of prenatal stress.

MONKEYS

As discussed above in the Rationale For Using Animals section, the WaRPRC AIDS-related research program has been using a tether-catheter system for several years to study viral infection, drugs, and vaccines in pregnant females and their fetuses. Some of this work has been criticized as having results concerning immunological, endocrinological, and pharmacological effects due to tethering alone, not to the actual experimental manipulations and substances involved in the research. This study will provide objective data concerning the extent to which tether-catheterization alone produces effects on these systems during pregnancy, as well as the degree to which the tethering method alone produces effects on the postnatal growth and behavioral development of offspring .

University of Washington **PRF-4**
Animal Care Committee

ANIMAL USE PROCEDURES:

Check "yes" or "no" for each item. If an item is checked "yes", provide a detailed description or justification (if required) for that item on the continuation page that follows. Please use the specifics listed in parenthesis as a guideline. In the description of your protocol, you must provide a specific timeline for all procedures including the endpoint of the study for each animal.

#	Yes	No	
1.	☒	☐	**Anesthesia** (agent, dose, route of administration, monitoring protocol, scavenging of waste gases)
2.	☐	☒	**Antibody production** (adjuvant used, amount, frequency, and route of administration, collection protocol, number of taps for ascites fluid, monitoring protocol)
3.	☒	☐	**Administration of drugs/reagents/cells/etc.** (agent, amount, route, and frequency of administration, anticipated side effects, monitoring protocol)
4.	☒	☐	**Behavioral testing** (stimuli, restraint, scientific justification for using noxious stimuli)
5.	☐	☒	**Potentially hazardous agent administration** (list radioactive, chemical, and biological agent(s), state dose, effects on animals, danger to humans, monitoring, precautions to protect personnel, special containment and disposal requirements)
6.	☒	☐	**Blood sampling** (method, site, volume, frequency)
7.	☒	☐	**Implanted catheters, prostheses, etc.** (site, type, monitoring protocol, maintenance and care of chronic implants)
8.	☐	☒	**Special diet or restriction of food or water** (amount, composition, duration, anticipated effects, justification for restriction)
9.	☐	☒	**Ether use** (justification for the use of ether, fume evacuation method, room used, storage method)
10.	☐	☒	**Euthanasia** (agent, method, criteria used to decide upon euthanasia, timepoint in study when euthanatized, scientific justification for methods not approved by the AVMA [*JAVMA* 202:229-249, 1993])

University of Washington **PRF-5**
Animal Care Committee
ANIMAL USE PROCEDURES (continued):

#	Yes	No	
11.	☐	☒	**Spontaneous death of animal, instead of euthanasia, as endpoint of the study** (written scientific justification required)
12.	☐	☒	**Paralytic agents** (agent, dose, route, monitoring protocol to insure adequate anesthesia)
13.	☐	☒	**Potentially painful procedure - list procedures that would be considered painful in the absence of anesthesia or analgesia** (how pain will be assessed, analgesia dose and frequency, written scientific justification is required if analgesics are to be withheld from animals with signs of pain)
14.	☒	☐	**Restraint** (method, frequency, duration, provide scientific justification if prolonged or painful, trapping or capture protocol)
15.	☐	☒	**Terminal surgery, no recovery from anesthesia** (describe surgical procedure, endpoint)
16.	☒	☐	**Survival surgery, _____ (# per each animal)** (describe procedure, preoperative protocol, aseptic precautions, monitoring, supportive care, duration, postoperative care, deficits. Provide scientific justification for multiple major survival surgeries on a single animal. Major surgery is defined as one that penetrates and exposes a body cavity or which produces a permanent impairment of physical or physiological functioning.)
17.	☒	☐	**Collection of tissues** (identity, method, timepoint of study that tissues are collected)
18.	☐	☒	**Tumor transplantation or induction** (type, site, functional deficits expected, tumor mass, metastasis, monitoring, endpoint)
19.	☐	☒	**Toxicity testing** (protocol, side effects expected, monitoring, endpoint)
20.	☐	☒	**Transgenic animal production** (methods, disposition of non-transgenics)
21.	☐	☒	**Are there any medications or procedures which should not be administered by veterinary personnel because they would render the results of the study invalid?** (Please list on continuation page)
22.	☐	☒	**If this study involves the use of nonhuman primates, will group housing be a component of an environmental enrichment program?** (If not, written scientific justification is required)

University of Washington
Animal Care Committee

PRF-6

ANIMAL USE PROCEDURES

Description, Justification

Use this page and add others as needed to describe the animal use procedures for any item checked "yes" on the previous two pages. Use the information in parenthesis as a guide for your response. **In the description of your protocol, you must provide a specific timeline for all procedures including the endpoint of the study for each animal.**

☐ I wish to withhold information that reveals the experimental hypothesis or design from release to the public under the Freedom of Information Act.

Item #	Description
1	Ketamine will be used for all femoral vein blood draws, flurothane for all ultrasound examinations for fetal viability and growth. Doses will be determined by WaRPRC veterinary staff.
3	See tethering-catheter procedures below
4	Offspring will be housed in the Infant Primate Research Laboratory (IPRL) according to the standard husbanry procedures including daily socialization periods in the playroom. The infants will receive the IPRL developmental test battery of growth, reflex, communication, social, emotional, memory, learning, and perception measures.
6	Blood will be drawn from pregnant female and fetal catheters four times each week (before and after noise stress test periods on Mondays and Fridays). Femoral vein blood will be drawn from all pregnant females once per week. Volumes will be approximately 3 ml for adult females and 1 ml for fetuses. These volumes have proven safe in prior tethering research. 1.5ml samples will be drawn from offspring at one month intervals from postnatal week 1 through month 9. CBCs taken from all samples will determine whether too much sampling has occurred for any given animal, although this is a very rare occurrence with these sample volumes and frequencies.
7	Tethering and catheterization will follow the standard procedures developed in the WaRPRC since 1987. Tether: The tether system is comprised of a lightweight nylon jacket attached to a flexible metal tether. The tether is then mounted to a ball bearing assembly attached to the external top of the animal's homecage. The entire assembly rotates and allows the animal to move freely throughout the homecage, while access is maintained for continuous physiological recording and intermittent sampling of maternal and fetal blood, maternal and fetal cardiovascular functioning, and amniotic fluid (Morton, et al., 1987). Jacketing: Mothers will be adapted to the nylon jacket and tether at 80-114 days gestation, starting approximately 4 weeks prior to surgery. Because a few mothers have difficulty adapting to the jacket prior to surgery, extra animals will be brought to the

IPRL to serve as a back up. Once the animals are adapted to the jacket, the extra animal will be returned to the breeding colony.

Surgery: At 115 days of gestation the animals will be sedated (Ketamine, 10 mg/kg IM) and prepped for surgery. For the surgery, animals are placed under isoflurane anesthesia. After anesthetic depth is established, a femoral vein and artery will be catheterized with PV 6 polyvinyl catheters. The catheters are inserted 15-17 cm, which places the tip above the iliac bifurcation but below the renal vein/caval-artery/aorta junction. The arterial line is used for blood pressure and acid/base monitoring during anesthesia. Lactated ringer's solution is given during surgery via a separate temporary IV line, not the implanted venous line placed at the end of surgery. Next, a paramedian pelvic laparectomy will be performed. Validation of cephalo/cervical fetal orientation will be established by internal rotation. Then a transverse supra-cervical incision will be made in the uterus. Amniotic fluid will be collected to decompress the uterine pressure and will subsequently be returned to the amniotic cavity at the conclusion of surgery. The fetal head will be exteriorized to the manubrium, and aliss tissue forceps will be used to attach the fetal skin to the uterine incision. A parapharyngeal incision will be made in the fetal neck and a PV-3 and PV-4 catheter will be inserted 20 - 30 mm into the carotid artery and internal jugular vein, respectively. The catheters will be anchored to the fetal skin closure, and the fetus will be returned to the uterus. Two amniotic "bird-cage" catheters will be placed into the fundus of the uterine cavity and the uterus will be tightly closed in three layers (amnion-chorion, myometrium, and serosa). The catheters exit the uterus through tight puncture holes in the uterine wall, not through the incision site. Purse string sutures around each individual catheter prevent fluid loss. Each catheter will be anchored to the uterus adjacent to the uterine incision, then the abdomen will be closed in layers and the catheters (maternal: femoral artery and vein; fetal: jugular vein, carotid artery and two in the amniotic cavity) will be tunneled subcutaneously to the midscapular region of the dam. The dam will then be placed in the tether system for unrestrained recovery in the IPRL.

Antibiotics and Postoperative care: Animals are treated approximately 1 hour before surgery with a prophylactic antibiotic (25/mg/kg cefazolin IM) and immediately after surgery with 25 mg/kg cefazolin IM, 50 mg iron dextran IM, and 1.0 ml vitamin B complex IM. Cefazolin a 1g/day IV is administered via a maternal saline bag for 7 days. Ketofen (5 mf/kd), an analgesic, is administered IM approximately 1 hour before removal of isoflurane anesthesia and continued for six hours for 2 days, or longer if necessary.

Tocylytics: In order to reduce the risk of abortion due to the surgery, tocylytic agents are always administered prophylactically during the first week and beyond if necessary. An intrauterine pressure monitor is used to indicate prelabor contractions. Once the fetus reaches gestational age 155, tocylytic drugs will not be used and labor will be allowed to proceed, once initiated. The incidence of labor in pregnant macaques on tocylytic agents throughout pregnancy is less than 10%. The tocylytics are administered as follows: Indomethacin, 25 mg BID with fruit is given for 5 days. Terbutaline at 2 mg/day for 2 days and at 1 mg/day for 3 subsequent days is given IV via a second maternal saline bag. Urine is checked daily for glucose and ketones. If they are found in the urine or uterine contractility is not suppressed with terbutaline, this drug is stopped and magnesium sulfate is started. A loading dose of 100 mg in 10 ml of saline is administered IV over 10-15 minutes followed by 53 mg/hour IV via a maternal saline bag. Plasma magnesium levels are checked pre-dosing and at 2 hours from

administration. Target plasma concentrations are 4-6 mEq/L, and IV magnesium sulfate is increased gradually until concentrations in this range are achieved. Plasma levels are checked every 2-3 hours until steady-state levels have been reached, and then daily until drug administration is stopped. Calcium chloride at 100 mg is administered IV in the event of a magnesium overdose. Animals are maintained on this regimen of magnesium sulfate for no longer than 4 days, and serum chemistry values are monitored daily. All saline solutions are co-infused with 3 U/ml heparin.

These procedures have been used in AIDS-related studies by at the WaRPRC for the past four years. After an initial "skill-honing" period, the tethering and catheter surgery procedures have produced liveborn infants in all cases over the past two years (12 out of 12 successes).

14 See tethering in #7 above

16 See Surgery in #7 above

17 Feces will be taken from cage pans once each week to assay steroid hormones of all females in the study under noninvasive procedures. These will be assayed in the UW OBGYN laboratory of Dr. Sam Wasser.

22 Nursery reared infant macaques must be housed individually in order to perform valid behavioral tests. When reared with mothers or peers, most individuals become very upset when separated for testing, and do not perform at all or perform well below their actual ability levels. During our tests, infants receive a great deal of human handling and are presented with interesting and challenging problems to solve. To insure good social development, all animals receive periods of 30 minutes per day, 5 days per week, with 4-5 other infants in a playroom environment. This has proven adequate to produce species-typical social development, with excellent juvenile and adult adaptive abilities when living in large social groups or in breeding groups. One possible alternative to this single cage, socialized, procedure would be to rear macaque infants in pairs. Unfortunately, research from the early 1960s and recent work in our laboratory has shown that pair rearing of infants results in abnormal clinging behaviors, reduced play behavior, increased passive behavior, and inability to adapt to social group housing as juveniles.

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals.

Intergenerational psychobiological processes are fundamental to understanding the organization of the developing fetus. Understanding pregnancy-related complications such as stress, prematurity, low birthweight, intrauterine growth retardation, stillbirths, and teratogens all rests on our ability to understand physiological processes of fetal development. In this study we will investigate prenatal psychological stress from gestational days 120- 155 using a maternal tethering system that will allow us chronic access to the blood supplies and physiological functioning of both the mother and the fetus. This access will enable us to simultaneously monitor the immune, endocrine and cardiovascular systems of both the mother and fetus immediately prior to, during, and following the presentation of unpredictable noise stimuli. Postnatally, the Infant Primate Research Laboratory (IPRL) procedures will be used to assess the physical, behavioral, and cognitive development of the offspring. Four study groups (6 female, 6 male fetuses/group) will include (1) tethered-noise stress, (2) tethered-no noise stress, (3) no tether-noise stress, (4) no tether-no noise stress.

Our study has a second goal. The chronic tethering system proposed for this project is being used for a wide range of studies including understanding the causes of pregnancy complications and the effects of teratogen exposure on fetal development. This system is currently used at the Regional Primate Research Center (WaRPRC) to investigate maternal fetal transmission of HIV/SIV. The tether and catheter system can allow blood and fluid sampling, as well as real-time physiological monitoring, without requiring anesthesia, or capture/restraint disturbance. However, the system itself is invasive and potentially stressful. No experimental data currently exists on the behavioral or physiological effects of the tethering system on either the pregnant female or on fetal and postnatal development of the offspring. This project will provide these data.

PERFORMANCE SITE(S) (*organization, city, state*)

Regional Primate Research Center, UW, Seattle, WA

June 18, 1996

Dr. Murray Robinovitch
Animal Care Committee
Department of Oral Biology Box 357132

Dr. Ron DiGiacomo
Department of Comparative Medicine Box 357190

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SUBJECT: Group Review Project #2187-16

Acute and Chronic Effects of Prenatal Tethering and Psychological Stress

Thank you for your assistance in reviewing this project application for the Animal Care Committee.

A copy of the project review form and related materials are enclosed. The review group should review the project to determine whether refinements can be made to the project and that all proposed animal use procedures are consistent with the regulations and guidelines that govern the use of animals. Also, you should make a determination as to which ACC category (I-III) that the project should be assigned.

After you have had a chance to read and discuss the protocol, you should submit questions or concerns you have regarding the protocol to the investigator. This is most effectively done by meeting with the investigator. A list of initial questions is attached and more may be forthcoming from other ACC members.

A chair of this review group should be designated and that person is responsible for writing a report with recommendations to the Committee (a guideline is enclosed) and presenting the report at the Animal Care Committee meeting. If you should need any assistance with scheduling or with developing your report please contact Tena Smith at 543-9678.

Review group reports are due by July 19, 1996, in order to be presented at the next Animal Care Committee meeting. The Committee meeting is scheduled for July 25, 1996, at 3:30 p.m., in the South Campus Center, Room 316L.

Please contact me at 543-3818 if you have any questions.

Steven Meyer
Animal Care Committee Coordinator Box 357190

cc: Dr. Sackett Box 357330
encl

JUN 25 1996

September 12, 1996

TO: Dr. Gene Sackett
Primate Center Box 357330

FROM: Tena Smith
Comparative Medicine Box 357190

SUBJECT: **Acute and Chronic Effects of Prenatal Tethering and Psychological Stress**

During review of your proposed project by the review group the following questions were raised:

1. Will appropriate postoperative analgesics be administered to the dam and will the analgesics provide pain relief for the fetus.

2. What is the nature of the "loud or surprising stimulation that frequently occurs in the BL-3 environment" and why can't it be eliminated so that the study can be limited to just the tether-catheter effect, thus halving the number of required animals.

3. Please provide a more detailed description of how you arrived at the number of animals to be used. Please provide information of variable(s) to be measured, expected differences to be detected, and level of significance and power.

4. Unless you are using some method to predict sex, won't you need some animals to compensate for the fact that it is unlikely to obtain a ratio of 50% males and 50% females?

5. Is it possible to have only three groups as follows:
   a. no tether
   b. tether
   c. tether-noise
   and eliminate the no tether-noise group?

6. Will untethered-uncatheterized, and tethered-catheterized females be anesthetized for all blood draws?

7. On page 6 item 7 of your project review form you speak of tocylytics. Will different macaques be given different and varying amounts of tocylytics? If so, will this amount confound the data?

8. Will untethered dams fetuses have catheters in place?

TO: ACC Review group for **Acute and Chronic Effects of Prenatal Tethering and Psychological Stress**
%Tena Smith
Comparative Medicine
Box 357190

FROM: Gene Sackett

Thank you for the opportunity to respond to your questions. I hope my answers provide the information you require.

(1) Postoperative analgesics to dam and fetus

At 115 days of gestation the animals will be sedated (Ketamine, 10 mg/kg IM) and prepped for surgery. For the surgery, animals are placed under isoflurane anesthesia. After anesthetic depth is established, a femoral vein and artery will be catheterized with PV 6 polyvinyl catheters. The catheters are inserted 15-17 cm, which places the tip above the iliac bifurcation but below the renal vein/caval-artery/aorta junction. The arterial line is used for blood pressure and acid/base monitoring during anesthesia. This procedure results in both maternal and fetal anesthesia, and has been developed over the past several years by the Primate Center Tether-Catheter surgical team headed by John Weyhrich (DVM) and Cliff Astley.

(2) What is the nature of the "loud ..." stimulation that occurs in the BSL-3 environment, and why can't it be eliminated .... (to) halve the number of subjects.

Unfortunately, my ACC form responses apparently did not adequately describe the rationale, aims, and nature of this study. First, the study is not actually about tethering. It is about prenatal psychological stress, an important concept that has almost no **experimental** support in human or nonhuman primates. With the exception of a few human and primate short term studies, there is no research documenting the acute effects of a repetitive prenatal stressor on both the mother and the fetus, and the degree of habituation of those effects over gestational time. Of equal importance, there are no studies documenting repetitive acute stress effects on consequent postnatal development of offspring. In fact, most human studies document psychological stress effects by anxiety questionnaires given after pregnancy is completed.

Over the past 8 years a team of primate researchers at the University of Wisconsin has been studying the effects of a prenatal "noise" stressor on postnatal offspring development. From about 100-140 days of gestation, 3 days per week, pregnant female rhesus monkeys are taken to an initially unfamiliar room. At unpredictable times over a 10 minute period, 3 loud (110 db) 1-sec bursts of 1300 Hz sound are presented. This procedure has resulted in lower birthweights, shorter gestations, delayed maturation of basic reflexes, lower play and affiliative social behavior with greater fearfulness, and delayed development of basic cognitive abilities. However, most of these measures exhibit sex differences, with males more severely affected than females. Furthermore, with the exception of cortisol and some hormone measures taken before and after the total stress period, no prenatal physiological measures are available to document the acute effects of the noise stressor.

We also studied prenatal stress in pigtailed monkeys. In this case the stressor was capture from the living cage and brief confinement to a transfer box once per day, 4-5 days per week, from 30-130 days of the 170 day gestation period. Females in the capture stress group lived in the same room. When the capture technician appeared in the room up to three times each day, the females would become highly aroused, vocalize, and shake their cages. A given female did not know when her turn would come for capture. With the exception of frequency, these conditions emulate the standard practices for taking pregnant females from

their living cages. These pregnancies were compared with those of females that were captured only three times during pregnancy.

Our pigtail macaque results were not all the same as those from rhesus macaques at Wisconsin. We did not find birthweight or gestation length effects, nor did we find effects on cognitive development. We did find effects on reflex maturation rate and social development. Also, like the Wisconsin studies, we found large sex differences, with stressed males showing greater effects than females. Like the Wisconsin studies, we did not have measures of acute effects of the stressor, except for some crossectional hormone and cortisol measures at 110 gestational days and at birth.

To our knowledge, the study we are proposing will be the first for any primate research-- on human or nonhuman primates-- to (1) measure acute physiological and behavioral effects of a prenatal psychological stressor on both the mother and the fetus, and (2) evaluate the extent of habituation of such acute effects over repeated presentation of the stressor and evaluate potential prenatal growth retardation effects, and (3) assess relationships between the degree of prenatal stress acute effects, habituation, and growth effects on postnatal growth, hormone, immune system, and behavior development. Such information is crucial for the numerous theories concerning prenatal psychological-social stress on postnatal development, as these theories all depend on the existence of important relationships between acute and chronic physiological stress responses and deviant postnatal maturation.

The technology allowing simultaneous measurement of maternal and fetal responses to potential stressors is tethering and catheterization. Unfortunately, tethering per se may have stress effects, although the precise effects and their extent and duration is not known from the previous studies which we have read. Furthermore, there is almost no information concerning the effects of maternal-fetal catherization and tethering on offspring postnatal development. This is where our study design has significance for the several past AIDs-related studies that have used this technique and for future work. This purpose, although very important as part of our project, is not any more important than the issues our work will address related to psychological stress and the possible interaction of psychological with tethering-catheterization stress.

With respect to BSL-3 "noise", that statement was simply one example of a practical problem associated with BSL-3 maternal-fetal research to date. Namely, adult animals have been housed in the same room as infants, due to chronic space shortages. When infants are handled by people, adult monkeys become upset and vocalize and shake their cages. This upsets the infants. Also, BSL-3 animals are handled often for blood draws and other procedures. This also results in a fair amount of noise from vocalizing and cage shaking, noise which can be heard throughout much of a BSL-3 area consisting of several rooms. In general, we have recently been able to house infants in separate rooms from adults, although adults may have to pass through the infant room on their way to various tests. This has cut down on at least some of the disturbances that were common in our BSL-3 until recently. We anticipate that future studies will be conducted under much better infant nursery rearing conditions when the new BSL-3 facility in the RR-wing 1st floor is completed. Infants and pregnant female husbandry will be conducted under the Infant Primate Laboratory conditions that we have developed over the past 26 years. This should eliminate most, if not all, of the potential "stress" artifacts that have been present in some prior BSL-3 studies. Our proposed study will be conducted in non-BSL-3 areas in the new RR space.

(3) Sample sizes, dependent measures, expected differences, statistical power

Our sample sizes are dictated by four factors: namely, the large sex differences found in our prior work and work at Wisconsin; our data on over 100 pregnant pigtail monkeys housed in the Infant Lab concerning average values and individual differences in pregnancy and stress hormone values before and after mating, during gestation, and at birth; longitudinal ultrasound growth data on over 40 pigtail fetuses and crossectional data on over 200 others; and 26 years of Infant Lab data on several hundred to over 1000 newborns and infants on labor and delivery measures, birthweights, ponderal and skeletal postnatal growth, and reflex, perception, motor, learning, cognitive, and social behavior measures.

We calculated that a minimum of 6 females and 6 males per group are required in our four groups to achieve medium power (40-60% likelihood of detecting significant differences) to detect effects between any pair among our four groups, with or without sex differences, on (1) ultrasound fetal development measures, (2) cortisol, progesterone, testosterone, and estrogens as measured from the tether on half of the sample, and from blood draws or noninvasively from feces on the total sample, (3) labor duration and quality and perinatal simian Apgar ratings, (4) birthweights and postnatal skeletal and ponderal growth, (5) neonatal reflex development, (6) learning and cognitive behavior tests, and (7) social-emotional development measures. We calculated high power (60-80% likelihood of detecting significant differences, n=24 per group) to detect effects of noise versus no noise and tethering versus no tethering with or without sex differences on these measures. We have no specific expectations concerning our proposed doppler ultrasound placental flow rate measures; behavioral and heart rate and blood pressure responses during noise stress tests; prenatal maternal and fetal or postnatal offspring CBC values, lymphocyte cell type numbers and percentages, cytotoxic cell numbers and percentages, and killing and other functional immune measures; or a MAXI panel screen of electrolytes and nutrients. However, on the basis of means and variances in prior AIDS-related work with these immune measures, we expect at least medium power to detect effects of noise versus no noise, tethering versus no tethering, and the interaction of sex with these noise and tethering factors.

(4) We will take an amniotic fluid sample during ultrasound testing at 60 gestational days, prior to the start of tether jacket adaptation at 80 days. We will determine sex from this sample, and assign animals randomly to other groups when the sex requirements of their prior random assignment have been met.

(5) As we detailed in question 2 above, the no tether-noise group is a critical component of this study. The noise psychological stress variable is actually the most important theoretical factor in the project and our primary reason for designing the project in the first place.

(6) All females in the study will be anesthetized for all procedures involving blood draws.

(7) Dams will be given tocylitics initially as a standard protocol, developed in AIDS-related research over the past 4 years. They will receive additional doses as a function of information from an intrauterine pressure monitor put in place at the time of surgery. Some females may require more or higher doses based on this information. Tocylitic dose amounts and durations will be used as correlates in exploratory analyses of this factor with our other measures. We will therefore be able to address the issue of how much variation in tocylitics may correlate with our various hormone, immune, and postnatal measures. If necessary, tocylitic dose will be used as a covariate in our primary analyses of tethering with versus mithout nosie stress. Please see below concerning the general issue of confounding in this study.

(8) Untethered dams' fetuses will not have catheters in place (see below).

Comments concerning potential confounds and possible controls.

This is a very complicated research area with very little prior experimental data in nonhuman primates or humans, and no longitudinal prenatal acute data predicting postnatal effects. Tethering and catheterization involve a number of potential individual factors which could influence prenatal and postnatal dependent variables. In fact, the noise stress procedure also involves a number of possible causal agents, including noise itself, being taken to a strange room, and anticipation of the procedure on any given day. At this point in knowledge, we are concerned with showing whether the overall procedures of tethering plus catheterization and/or noise stress testing have acute effects which do not habituate, which areas of measurement show these effects, whether or not these prenatal effects predict any postnatal differences, and if there is prenatal-postnatal prediction, which postnatal measures are involved. These data will show us which stress procedures, if any, require further study. They will also show which procedures, if any, need to be controlled for or modified in AIDS-related research to obtain results that are not confounded by procedural, stress, or psychological factors. The specific modifications necessary may depend on future studies. We believe that the 48 animals to be studied over a four year period are a reasonable number given the important implications of this work for theories of psychological-social stress and for practical matters concerning factors which need to be controlled in AIDS-related and other invasive prenatal research involving potential psychological and/or physical stressors..

UNIVERSITY OF WASHINGTON
Animal Care Committee

REVIEW GROUP REPORTING FORMAT

Please use this format when preparing project reviews for presentation at the ACC meetings.

ACC review #_____ACC meeting date_____

Review Group Members_____

==========

RATIONALE/SIGNIFICANCE OF THE PROPOSED PROJECT:

METHODS/EXPERIMENTAL PROCEDURES OF PROPOSED PROJECT:

CONCERNS RAISED BY REVIEWERS AND/OR ACC MEMBERS AND PI'S RESPONSE:

==========

REVIEW GROUP FINAL DISPOSITIONS:

Category I, II, or III?

Approval
Approval with modifications stated
Further review
Withhold approval

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FIFTY YEARS

HEALING

Department of
Comparative Medicine

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Seattle, WA 98195-7190
Phone: (206) 543-8047
Fax: (206) 685-3006

June 7, 1996

To : Mr. Steven Meyer
ACC Coordinator

From : Melvin B. Dennis, Jr., D.V.M. Melvin B Dennis Jr.
Professor & Chairman

SUBJECT: IACUC Review of Protocol 2187-16

I am calling for full IACUC review of protocol 2187-16 "Acute and chronic effects of prenatal tethering and psychological stress". My concerns center on the question as to whether what will be learned from the study is worth what the animals will be put through to collect the data. The specific questions that occur to me include:

1. Part of the search for alternatives should include assessment as to whether the proposed studies could be done on other animals. This includes not only looking for less sentient animals, but looking for animals that may have similar procedures being done for other studies. The last paragraph under item 7 of the PRF states that the surgical procedures have been done at the WaRPRC for the past 4 years. Why can't the proposed studies be done on these animals?

2. If there are reasons that the study can't be performed as suggested in question 1, at least this study would seem more defensible to me if it was to be done as a control group for one of the AIDS-related studies they allude to, where similar procedures are done.

3. Perhaps this question is just another way of stating question 2, but on page 3 of the PRF it is stated that there are no available data concerning the effects of tethering & catheterization alone on pregnancy, and fetal and postnatal development. Is the rationale for doing the proposed study, then, that it would become a control group for other studies? The problem is that they would be historical, rather than concurrent controls and similar studies would be required for the subsequent studies. Why not do study on concurrent controls for a study such as the one referred to in the last paragraph of item 7?

4. On the bottom of page 3, they refer to 48 animals in 4 groups of 12. What are the other groups? 48 animals are a lot to establish a proposed baseline.

5. How will stress be measured and how will effects of surgery & catheterization on stress be separated from confounders, such as administration of indomethacin, terbutaline, magnesium sulfate, ketamine, noise stress tests, etc.?

6. It is stated that there are data from their group and others regarding the effects of prenatal stress on fetal and postnatal development. Certainly there must be data on the effects of tethering and catheterization, so why can't extrapolation regarding the effects of both be used to give an indication, that could then be confirmed in the control group of other studies?

7. "Ketofen (5mf/kd)" is listed on PRF page 7, ??

8. What happens to the fetal catheters during the birthing process? Will caesareans be performed?

UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE

Department of
Comparative Medicine

Mailstop SB-42
T-142 Health Sciences Center
Seattle, WA 98195
Phone: (206) 543-8047
Fax: (206) 685-3006

June 18, 1996

To: Dr. Gene P. Sackett
Psychology - Regional Primate Research Center
Box 357330

From: Steven Meyer
Animal Care Committee Coordinator
Box 357190

Subject: Animal Care Committee Review

Your project, "Acute and Chronic Effects of Prenatal Tethering and Psychological Stress" has been designated for full committee review by the Animal Care Committee. A review group has been assigned to review your project and give their recommendations to the Committee. The review group will be contacting you concerning their review of your proposal.

Please contact me at 543-3818 if you have any questions. Thank you.

cc: ACC Review Group
attch

January 23, 1997

TO: Dr. Gene Sackett
Primate Center, Box 357330

SUBJECT: **Acute and Chronic Effects of Prenatal Tethering and Psychological Stress, ACC #2187-16**

Your protocol has been resubmitted to the Committee as amended, and will not be group reviewed unless called for by an ACC member.

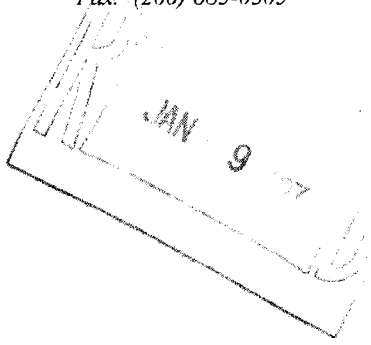
Sincerely,

Melvin B. Dennis, Jr., D.V.M.
Executive Secretary, Animal Care Committee
MBD:ts

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

Gene P. Sackett, Ph.D.
Regional Primate Research Center
E-mail: jsackett@bart.rprc.washington.edu

I-421 Health Sciences Center, Box 357330
Telephone: (206) 543-0440
Fax: (206) 685-0305



January 8, 1997

ACC Committee for Psychological Stress and Tethering Project
Dr. Melvin Dennis, Dr. Murray Robinovitch, Dr. Bernard Buetow
% Tena Smith
Comparative Medicine, Box 357190

Dear Committee:

Enclosed is the "pink sheet" peer review critique for my project on Psychological Stress and Tethering. The project will be funded, with an outstanding rating, but with elimination of the two conditions involving noise stress stimulation. In terms of the original application the following changes will be made.

(1) The title will be changed to *Acute and Chronic Effects of Prenatal Tethering.*

(2) The tethering + noise stress and the no tethering + noise stress groups will not be studied.

This leaves the design and methodology identical to the original application with respect to the remaining two test groups, sample sizes, test conditions, and measures. A summary of these features detailed in the original application and subsequent letter is as follows.

(1) Two groups will be studied. Tether group: mothers and fetuses will receive blood and amniotic fluid sampling catheters during surgeries at 115 days of gestation. No- tether group: will experience the same environmental conditions, but will not receive surgery, tethering, or catheterization. All newborns will be reared in the Infant Primate Laboratory under standard conditions, receiving the standard battery of growth and behavioral measures during infancy.

(2) Sample sizes will remain 6 females and 6 males per group, as approved and seen as well justified by the review committee.

(3) Venous blood samples will be taken from <u>all</u> pregnant females weekly, and ultrasound examinations for fetal growth and blood flow measures will be taken periodically before tethering, during the tethering adaptation period, and during the tethering period to 155 days of pregnancy.

(4) Immune system, nutrient, and hormone measures will be taken from catheter samples on tethered females and fetuses, and from venous blood draws and fecal samples on all females. Hormone, nutrient, and immune blood samples will be taken monthly during the postnatal follow-up period on the infants.

Thank you for your time and effort with this project,

Very Truly Yours,

Gene P. Sackett
Professor, Psychology

Core Research Project 1 of Dr. Sackett: Acute and Chronic Effects of Prenatal Tethering and Psychological Stress

Description: Understanding pregnancy-related complications such as stress, prematurity, low birthweight, intrauterine growth retardation, stillbirths, and teratogens all rest on an ability to understand physiological processes of fetal development. This study will investigate prenatal psychological stress in pig-tailed macaques from gestational days 120-155 using a maternal tethering system that will allow chronic access to the blood supplies and physiological functioning of both the mother and the fetus. This will enable simultaneous monitoring of the immune, endocrine, and cardiovascular systems of both the mother and fetus immediately prior to, during, and following the presentation of unpredictable noise stimuli. Postnatally, the Infant Primate Research Laboratory procedures will be used to assess the physical, behavioral, and cognitive development of the offspring. The study will also assess the effects of chronic tethering that is being used for a wide range of studies, including some at this Center to investigate maternal fetal transmission of HIV/SIV. The tether system itself is invasive and potentially stressful. No experimental data currently exists on the behavioral or physiological effects of the tethering system on either the pregnant female or on fetal and postnatal development of the offspring.

Critique: This project has a number of strengths. The work is in alignment with the goals of the Center, the Center facilities are uniquely suited to support the study, and it is a logical extension of other work done by the investigator. The study is well designed and the methodology will answer the questions of interest. The combined use of behavioral, cardiovascular, endocrine, and immune measures from both the mother and the fetus will generate a very comprehensive set of information to thoroughly evaluate the system being tested. The investigators have generated a broad base of

normative data for a number of the variables being examined. The relatively large sample size for each cell in the experiment is well-justified. Since the tethering technique being studied is applied in a variety of experimental situations, including some at this Center, characterizing the maternal and fetal consequences of the protocol will have great relevance to proper interpretation of findings from a variety of other investigations.

Some minor weaknesses are noted. There are no clear hypotheses being tested regarding the effects of the noise stressor or the tethering on any of the many dependent measures being collected. The rationale for using noise as a psychological stressor is not fully explained; nor is the relevance of that stressor to colony management procedures. There appears to be a lack of integration between this study and others on site, since at least some of the subjects of this study could be simultaneously participating on other protocols, and this would result in a cost savings to this project. There is no detail given on data collection techniques, the amount of data collected, etc. for the behavioral assessments of the mothers to be made before, during, and after the noise stress tests. And, although attention has obviously been paid to methodological issues that will make robust statistical analysis of the data possible, there is no detail given for the types of statistical comparisons to be made. The aspects of the project related to studying the noise stressor are eliminated with corresponding budgetary reductions. The merit of the project after these alterations is outstanding.

Investigator: Gene Sackett, PhD will serve as the project PI. He is exceedingly well qualified to perform this project. Dr. Sackett received his PhD degree from Claremont Graduate School in 1963 in psychology. He came to the WaRPRC from Wisconsin in 1970 and has been on the core staff since that time. In 1974 until present, he has been the Associate Director for Behavioral Research, Child Development and Mental Retardation Center. Dr. Sackett has written extensively within the area of nonhuman primate development and neonatology. Dr. Sackett would spend a modest amount of time overseeing the work, and a half time research technician and student assistant are also needed.

Budget: The following reductions are recommended during all five years of support due to the reduced workload resulting from eliminating the noise-testing aspects of the study. One 50% Research Technologist is eliminated. The supply items associated with tethering should be reduced by half (tocylytics, tether supports, and surgical supplies). In Other Expenses, all items associated with Project 1 should be reduced by half. In Year 1 the white noise generator and the electrocardiogram recorder are eliminated. In Year 5, there should be an $8,000 dollar reduction in the proposed personnel budget as the technician working with the tethered animals is no longer required.

January 14, 1997

TO: Dr. Gene Sackett
Primate Center, Box 357330

SUBJECT: **Acute and Chronic Effects of Prenatal Tethering and Psychological Stress**

The group review committee has the following remaining questions regarding you protocol:

1. What will happen to the fetal catheters during birth?

2. Please clarify whether 12 animals will be used in 2 groups with 6 animals per group, or 12 animals per group totaling 24 animals.

Please respond in writing to me or to the Animal Care Committee Coordinator, Tena Smith (543-9678), at Comparative Medicine, Box 357190. Approval of your project cannot be granted until receipt and acceptance of your response by the Committee. Thank you.

Melvin B. Dennis, Jr., D.V.M.
Executive Secretary, Animal Care Committee

MBD:ts

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

Gene P. Sackett, Ph.D.
Regional Primate Research Center
E-mail: jsackett@bart.rprc.washington.edu

I-421 Health Sciences Center, Box 357330
Telephone: (206) 543-0440
Fax: (206) 685-0305

JAN 16 19

January 15, 1997

Dr. Melvin Dennis
Executive Secretary ACC
T-142 HSC
Box 357190

Dear Dr. Dennis:

Regarding your letter of January 14 concerning two pieces of information about our project "Acute and Chronic Effects of Prenatal Tethering", the answers are as follows.

(1) A delivery team will be called to the campus when an observer, watching a video monitor at least once per 30 minutes, observes a female showing signs of labor. That team separates the mother and newborn and removes the newborn's catheter manually. This procedure is the standard RPRC practice, developed over the past five years. It has resulted in no bleeding or infection problems.

(2) There will be two groups, each containing 12 animals, 6 females and 6 males. Thus, 24 animals will be tested in total. This was viewed as adequate by the scientific review group. Please note that past work here and elsewhere suggests that there may be sex differences in the prenatal and postnatal effects of prenatal interventions in a study such as this one. Six animals of each sex in the tethered and in the nontethered groups is not an excessive number, but does provide good statistical power for most of our measures.

Very Truly Yours,

Gene P. Sackett
Professor, Psychology

Date sent: **Wed, 8 Jan 1997 08:47:22 -0800 (PST)**
From: **Murray Robinovitch <robino@u.washington.edu>**
To: **Mel Dennis <mdennis@cmed1.cmo.washington.edu>**
Copies to: **JIM SACKETT <jsackett@bart.rprc.washington.edu>, bbuetow@cmed1.cmo.washington.edu**
Subject: **Re: Stress Project**

Thanks for jumping in Mel.

Murray R. Robinovitch
Professor and Chairman
Department of Oral Biology
Box 357132
University of Washington
robino@u.washington.edu
(206) 543-5477

On Tue, 7 Jan 1997, Mel Dennis wrote:

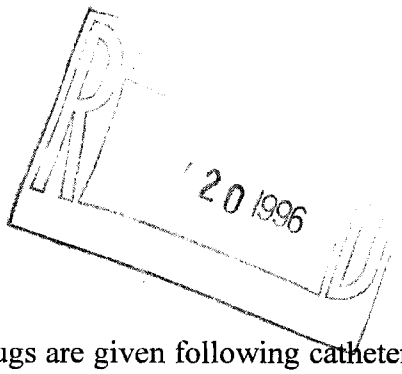
> Jim,
> We need to be able to see what groups remain, what is proposed for
> each group, and a statement that noise stress is not going to be
> administered. I don't feel strongly that a new ACC proposal is
> necessary if it can be clearly stated in a letter. However, if you
> have it on a disk, it may be easiest to edit it and submit it as a
> new application.
>
> Mel
> ---
> Date: Tue, 7 Jan 1997 16:21:19 -0800 (PST)
> From: Murray Robinovitch <robino@u.washington.edu>
> To: JIM SACKETT <jsackett@bart.rprc.washington.edu>
> Cc: bbuetow@cmed1.cmo.washington.edu, mdennis@cmed.cmo.washington.e
> Subject: Re: Stress Project
>
> Thank you for notifying us. I don't think that it is necessary to
> re-submit a new A.C.C. application, but I think it would be helpful if you
> would send Mel a copy of the pink sheet. If he thinks a new A.C.C.
> application is necessary, he can respond to these email messages.
> Otherwise, I will contact him and see if we can wind this up. Thanks again
> for your cooperation.
>
> Murray R. Robinovitch

> Professor and Chairman
> Department of Oral Biology
> Box 357132
> University of Washington
> robino@u.washington.edu
> (206) 543-5477
>
> On Tue, 7 Jan 1997, JIM SACKETT wrote:
>
> > Dear Committee:
> >
> > I have received the "pink" sheets for our Stress project from NIH.
> > The review was "outstanding", but they cut all of the noise stress
> > procedures. We are left with the tethering and no tethering
> > controls, at the requested sample sizes of 6 females and 6 males
> > per group. All other procedures involving treatments, husbandry, and
> > postnatal followup were as requested.
> >
> > Should I submit a new ACC proposal? Will this change the status of
> > the ACC proposal?
> >
> > Thanks for your efforts so far. I will do your bidding post haste.
> >
> > Jim Sackett
> >
>
> Melvin B. Dennis Jr., D.V.M.
> Professor and Chairman
> Department of Comparative Medicine
> Box 357190
> School of Medicine
> University of Washington
> Seattle, WA 98195-7190
> Phone: (206) 543-8047
> FAX: (206) 685-3006
> mdennis@cmed.cmo.washington.edu
>

21876

TO: ACC Review group for **Acute and Chronic Effects of Prenatal Tethering and Psychological Stress**
%Tena Smith
Comparative Medicine
Box 357190

FROM: Gene Sackett
Primate Center
Box 357330



RE: Postoperative Analgesia Procedures

Two combination antiinflammatory-analgesic drugs are given following catheter implantation surgery. The procedures follow the recommendations of the Primate Center Veterinary staff, and have been developed and tested in AIDS-related studies over the past 4-5 years..

The first drug is KETOFEN (Aveco). It is given i.m. every 6 hours for a minimum of three days. It is stopped after the female has returned to normal postures and activity patterns, as well as normal appetite. Normal is defined in terms of the very close observation of the animal during the two month tethering adaptation phase. The drug can usually be stopped after three days, but may take as many as five or six for a few animals.

The second drug is INDOMETHACIN (Lederle). The capsule contents are sprinkled in fruit and fed to the animal twice daily for five postoperative days. It is used along with KETOFEN because of its imputed muscle relaxation properties.

University of Washington
Records Management Services

December 20, 2007

Disposition Notification

Accession #	Accession Date	Record Group	
03 a 031	2/6/2003	/03/01/02/	National Primate Research Center: Animal Records

Record Series - Veterinary Charts 97-12-58188

ID #	Box #		Box End Date	Retention	Scheduled Disp Date
67365	01	Death Records (M75207 - J88333)	12/31/2001	5	12/31/2006
67366	02	Death Records (88357 - F91030)	12/31/2001	5	12/31/2006
67367	03	Death Records (91036 - 92271)	12/31/2001	5	12/31/2006
67368	04	Death Records (92218 - 94070)	12/31/2001	5	12/31/2006
67369	05	Death Records (94072 - M96120)	12/31/2001	5	12/31/2006

Number of boxes for this series - 5

Archivist's Comments

08 D 081
Disposition Number

Peggy Smith
Department Approval-Print Name

Andrea L Wa 1/25/08
Disposition Assignment Verification Date

Peggy Smith 1-18-08
Approval Signature Date

Barbara Benson 2/21/08
URC Verification Date

Please return to Records Management Services at Box 354910

Master History Report Printed on 8-Apr-2009 for user CAROLE

F91396 M. nemestrina Female Sire: T81051 Dam: 89109
Birth date: 16-DEC-91
Departure date: 17-MAY-01
Disposition: Euthanasia, experimental
Inbreeding coefficient: .000
Inbreeding history: .000 due to dam: .000 due to sire: .000
Breeding index: 3 Generation index: 1.750
*** No Case summary available ***
Ear tag: M-Y
Place of origin: WaNPRC at Medical Lake Field Station
Age at departure on 17-MAY-01 9.42 years (3440 days)
Femur length at birth: 60 mm
Separated from dam on: 29-MAY-92 Reason: standard protocol
Remarks: RECORD ARCHIVED WITH 2001 DEATHS

*** Gestational Information ***
Parity, all conceptions: 3
Parity, term pregnancies: 2
Gestational age: 163 days.

Seq	Mated	Separ.	K	Tested	T	R	Conc.	Term.	TC	TR
40	28-FEB-91	15-NOV-91		05-AUG-91	U	P	06-JUL-91	16-DEC-91	K	NV

First weight: 17-DEC-91 0 0.355 Kg.

*** Full Virus Test Summary ***

Virus	Target	R	Method	Date	Lab
3214 CHV-1 (B virus), Cercopith	antibody	-	Elisa Test	12-OCT-92	Southwes
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	20-JAN-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	20-JAN-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	20-JAN-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	20-JAN-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	20-JAN-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	09-FEB-98	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	06-OCT-98	UW SeaDL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	18-JAN-99	UW SeaDL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	01-FEB-99	UW SeaDL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	08-MAR-01	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	08-MAR-01	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	virus	-	Viral Cell Culture	08-MAR-01	NIH-BVRL
3214 CHV-1 (B virus), Cercopith	antibody	+	Elisa Test	08-MAR-01	NIH-BVRL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	02-OCT-92	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	19-OCT-92	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	19-OCT-92	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	19-JAN-93	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	19-JAN-93	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	14-JUN-93	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	14-JUN-93	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	19-NOV-93	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	19-NOV-93	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	10-MAY-94	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	30-NOV-94	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	30-NOV-94	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	01-AUG-95	PFS VL
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	02-AUG-95	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	17-JAN-96	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	14-MAR-96	PFS VL
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	15-SEP-97	SRV Sea
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	15-SEP-97	SRV Sea
3903 SRV-2 (Type D / Washington	antibody	-	Elisa Test	06-NOV-97	SRV Sea
3903 SRV-2 (Type D / Washington	virus	-	Raji Cell Culture	06-NOV-97	SRV Sea
3903 SRV-2 (Type D / Washington	viral DNA	-	PCR (Polymerase Cha	01-APR-98	UW SeaDL

Master History Report Printed on 8-Apr-2009 for user CAROLE

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3903 SRV-2 (Type D / Washington antibody     - Elisa Test          01-APR-98 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          06-OCT-98 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 06-OCT-98 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          18-JAN-99 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 18-JAN-99 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          01-FEB-99 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 01-FEB-99 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 14-JUN-99 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          14-JUN-99 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 25-OCT-99 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          25-OCT-99 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          02-MAY-00 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 02-MAY-00 UW SeaDL
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          18-JUL-00 AM Thoul
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 18-JUL-00 AM Thoul
3903 SRV-2 (Type D / Washington antibody     - Elisa Test          26-DEC-00 UW SeaDL
3903 SRV-2 (Type D / Washington viral DNA    - PCR (Polymerase Cha 26-DEC-00 UW SeaDL
3904 STLV-I                      antibody    - Elisa Test          29-SEP-97 VRL
3904 STLV-I                      antibody    - Elisa Test          25-OCT-99 UW SeaDL
3904 STLV-I                      antibody    - Elisa Test          02-MAY-00 AM Thoul
3904 STLV-I                      antibody    - Elisa Test          18-JUL-00 AM Thoul
3904 STLV-I                      antibody    - Elisa Test          25-SEP-00 UW SeaDL
3904 STLV-I                      antibody    - Elisa Test          26-DEC-00 UW SeaDL
```

*** Moves *** (All 45 Records)

Date	Seq	Room	Cage	Type-housing	Reason
16-DEC-91	0	B232	H	dam-infant pair in ca	Dam/infant bonding-obs
17-JAN-92	0	A225		group (more than 2)	permanent housing
29-MAY-92	0	A225		group (more than 2)	weaning
27-JUL-92	0	A132	D	group (more than 2)	research assignment
03-AUG-92	0	A218		group (more than 2)	
01-OCT-92	0	Q2	Q	single animal cage	research assignment
12-OCT-92	0	X2	J	group (more than 2)	research assignment
06-NOV-92	0	X2	W	group (more than 2)	temporary hold
	Why held: REPAIR WORK				
10-NOV-92	0	B224		group (more than 2)	permanent housing
15-NOV-92	0	B222		group (more than 2)	
07-DEC-92	0	B224		group (more than 2)	
08-JAN-93	0	B226		group (more than 2)	permanent housing
11-FEB-93	0	C213		group (more than 2)	permanent housing
23-MAR-93	0	C219		group (more than 2)	
12-APR-93	0	C217		group (more than 2)	
05-AUG-93	0	C219		group (more than 2)	
09-DEC-93	0	C217		group (more than 2)	
24-JAN-94	0	C215		group (more than 2)	
10-MAR-94	0	C221		group (more than 2)	
25-APR-94	0	C217		group (more than 2)	
22-JUN-94	0	C215		group (more than 2)	
08-SEP-94	0	C232		group (more than 2)	
15-MAY-95	0	B132		group (more than 2)	
19-JUN-95	0	C232		group (more than 2)	
13-NOV-95	0	C114		group (more than 2)	permanent housing
17-JAN-96	0	B132		single animal cage	permanent housing
07-FEB-96	0	C132		group (more than 2)	permanent housing
14-MAR-96	0	B232	I	single animal cage	Hold for shipment
03-APR-96	0	TRUCK		single animal cage	Hold for shipment
03-APR-96	10	I723		group (more than 2)	permanent housing
09-JAN-97	0	I725		group (more than 2)	permanent housing
05-DEC-97	0	RR159	2	single animal cage	research assignment
07-APR-98	0	RR159	3A	single animal cage	research assignment
23-APR-98	0	I720	3	single animal cage	permanent housing

16-JUN-98	0	I725		group (more than 2)	permanent housing
19-JAN-99	0	I728	2	single animal cage	clinical treatment
01-FEB-99	0	I725		group (more than 2)	permanent housing
11-MAY-00	0	I729		group (more than 2)	permanent housing
30-MAY-00	0	I734	5	single animal cage	permanent housing
31-MAY-00	20	I728	5	single animal cage	permanent housing
07-SEP-00	0	I728	7	single animal cage	permanent housing
28-SEP-00	0	I728	9	single animal cage	permanent housing
25-APR-01	0	I732	1	single animal cage	permanent housing
03-MAY-01	0	I567	17	single animal cage	permanent housing
17-MAY-01	20	DEAD			

*** Weights *** (All 66 Records)

Date	Seq	Weight
17-DEC-91	0	0.355 Kg
19-DEC-91	0	0.348 Kg
23-DEC-91	0	0.353 Kg
26-DEC-91	0	0.359 Kg
20-FEB-92	0	0.600 Kg
29-MAY-92	0	0.995 Kg
09-JUN-92	0	1.030 Kg
22-JUN-92	0	1.010 Kg
13-JUL-92	0	1.020 Kg
22-JUL-92	0	1.040 Kg
27-JUL-92	0	1.990 Kg
07-AUG-92	0	1.510 Kg
07-SEP-92	0	1.180 Kg
01-OCT-92	0	1.290 Kg
26-OCT-92	0	1.370 Kg
23-NOV-92	0	1.450 Kg
31-DEC-92	0	1.580 Kg
07-JAN-93	0	1.610 Kg
19-JAN-93	0	1.780 Kg
12-APR-93	0	1.990 Kg
14-JUN-93	0	2.100 Kg
18-NOV-93	0	2.510 Kg
20-JAN-94	0	2.700 Kg
10-MAY-94	0	2.990 Kg
30-NOV-94	0	3.520 Kg
02-AUG-95	0	4.090 Kg
13-NOV-95	0	4.400 Kg
17-JAN-96	0	4.460 Kg
14-MAR-96	0	4.370 Kg
22-JUL-96	0	4.800 Kg
30-SEP-96	0	6.000 Kg
26-MAR-97	0	4.600 Kg
15-SEP-97	0	5.200 Kg
06-NOV-97	0	5.000 Kg
16-DEC-97	0	5.300 Kg
11-FEB-98	0	6.400 Kg
01-APR-98	0	6.150 Kg
17-APR-98	0	6.000 Kg
29-JUN-98	0	5.400 Kg
25-AUG-98	0	5.400 Kg
06-OCT-98	0	6.000 Kg
30-NOV-98	0	6.800 Kg
13-DEC-98	0	7.000 Kg
20-JAN-99	0	6.400 Kg
01-FEB-99	0	6.600 Kg
22-MAR-99	0	5.800 Kg
26-APR-99	0	5.800 Kg

14-JUN-99	0	6.600 Kg
26-JUL-99	0	7.000 Kg
31-AUG-99	0	7.600 Kg
08-DEC-99	0	6.150 Kg
05-APR-00	0	7.600 Kg
06-APR-00	0	7.300 Kg
18-APR-00	0	7.600 Kg
02-MAY-00	0	7.000 Kg
09-MAY-00	0	7.000 Kg
18-JUL-00	0	7.200 Kg
25-SEP-00	0	7.400 Kg
07-NOV-00	0	7.800 Kg
16-NOV-00	0	7.800 Kg
15-DEC-00	0	7.800 Kg
26-DEC-00	0	7.800 Kg
12-JAN-01	0	8.000 Kg
09-FEB-01	0	8.000 Kg
08-MAR-01	0	8.400 Kg
10-MAY-01	0	8.980 Kg

*** Tb Tests *** (All 24 Records)

Date	Seq	Where	Ketamine	Atropine	Other-drug	R24	R48	R72	T
29-MAY-92	1	left lid							m
29-MAY-92	2	right lid			PPD				
26-OCT-92	0								
19-JAN-93	0								
12-APR-93	1	left lid							
14-JUN-93	1	left lid							
18-NOV-93	0	left lid							
20-JAN-94	0	left lid							
10-MAY-94	0	left lid							
30-NOV-94	1	left lid							
22-MAR-95	1	left lid	50 Mg	.250 Mg					
02-AUG-95	0	left lid	40 Mg	.250 Mg					
13-NOV-95	0	left lid	50 Mg	.250 Mg					
17-JAN-96	0		40 Mg	.200 Mg		1	1	1	
14-MAR-96	0					1	1	1	
22-JUL-96	0	left lid				1	1	1	m
30-SEP-96	0	left lid				1	1	1	m
15-SEP-97	0	right lid				1	1	1	m
16-DEC-97	0	right lid				1	1	1	m
01-FEB-99	0	right lid				2	1	1	m
14-JUN-99	0	left lid				1	1	1	m
08-DEC-99	0	right lid				1	1	1	m
18-JUL-00	0	left lid				2	1	1	m
26-DEC-00	0	right lid				2	2	2	m

*** Project Records *** (All 9 Assignments)

Assigned	Returned	Investigator	Pg	Pj	Use	Acc	Expires	Title
16-DEC-91	28-JAN-93	Breeding/Reserve	00	00				Medical Lake Breeding Project
01-OCT-92	28-JAN-93	SAIDS Research	66	20	No Biologic Change	2409-43	30-MAY-98	Screening SRV-Free Mn and Pc
29-JAN-93	30-APR-93	SAIDS Research	66	17	No Biologic Change			SRV-Free Breeding Colony
01-MAY-93	16-NOV-97	Breeding	51	05	No Biologic Change	4027-05	10-OCT-08	Breeding/Breeder Virus-Free
17-NOV-97	04-DEC-97	Breeding	51	05	Hold For Project	4027-05	10-OCT-08	Breeding/Breeder Virus-Free
05-DEC-97	15-APR-98	Sackett, Gene P.	46	01	Permanent Biologic Change	2187-16	26-OCT-01	Acute and Chronic Effects of Prenatal Tethering and Catherization
		Comment: Tethered with fetal catheterization						
16-APR-98	23-OCT-00	Breeding	51	05	No Biologic Change	4027-05	10-OCT-08	Breeding/Breeder Virus-Free
28-SEP-00	23-OCT-00	Morton, William R.	88	05	Screening	2409-68		Evaluation of osteoinductive material in non-human primate osteop

Master History Report Printed on 8-Apr-2009 for user CAROLE

24-OCT-00 Morton, William R. 88 05 Terminal 2409-68 Evaluation of osteoinductive material in non-human primate osteop

*** Breeding Records *** (All 10 Records)

Seq	Sire (TuID)	Mated	Separ.	K	Tested	T	R	Conc.	Term.	TC	TR	Infant(TuID)
10	91169	03-APR-96	21-OCT-96		22-JUL-96	P	P		24-NOV-96	E	NV	J96283
20	U		22-SEP-97		15-SEP-97	U	N					
30	97074	22-SEP-97	05-DEC-97		06-NOV-97	U	P	17-OCT-97	24-MAR-98	E	EV	J98059
40	97074				29-JUN-98	U	N					
50	97074				25-AUG-98	U	P	21-JUL-98	18-JAN-99	E	NV	J99016
60	97074				22-MAR-99	U	N					
70	97074				26-APR-99	U	P	17-MAR-99	10-SEP-99	K	NV	J99252
80	97074				08-DEC-99	U	P	06-NOV-99	01-MAY-00	K	NV	J00107
	Comment:Ultrasound 4/5/00 EGA 152 Ultrasound 4/18/00 EGA 165 (vertex)											
90	97074				02-MAY-00	U	N					
100	97074				09-MAY-00	U	N					

*** Blood Draws *** (All 14 Records)

Date	Site	Reason	What Drawn	Where Drawn	Amount	By	SB	Investigator	Pg	Pj
01-OCT-92	ML	Research	Blood	Rt. Femoral	5.0			SAIDS Research	66	17
19-JAN-93	ML	Research	Blood	Rt. Femoral	5.0			SAIDS Research	66	17
14-JUN-93	ML	PI	Blood	Rt. Femoral	5.0			SAIDS Research	66	20
18-NOV-93	ML	PI	Blood	Rt. Femoral	3.0			SAIDS Research	66	20
10-MAY-94	ML	Other	Blood	Both Femorals	5.0			Tissue Program		
30-NOV-94	ML	Other	Blood	Both Femorals	7.0	DW-LA		Tissue Program		
02-AUG-95	ML	Diagnostic	Blood	Lf. Femoral	3.0	GK				
	Comment: Colony SAIDS screen									
17-JAN-96	ML	Diagnostic	Blood	Rt. Femoral	3.0	JM		SAIDS Research	00	00
06-OCT-98	Colony	Diagnostic	Blood	Rt. Femoral	2.5	KE				
	Comment: SRV TESTS									
14-JUN-99	Colony	Diagnostic	Blood	Rt. Femoral	2.5	KE				
	Comment: SRV									
18-APR-00	Colony	Research	Blood	Rt. Femoral	10.0	JT		Southwest Foundation		
18-JUL-00	Colony	Diagnostic	Blood		5.0					
	Comment: with TB test									
25-SEP-00	Colony	Diagnostic	Blood	Rt. Femoral	5.0					
26-DEC-00	Colony	Diagnostic	Blood	Rt. Femoral	4.0					
	Comment: with TB test									

*** Hematologies *** (All 16 Records)

OPTIONS: Differential data are reported here as absolute counts.

Animal	Tested	HEMO	PCV	RBC	MCH	MCV	MCHC	IM	RET	ORC	PL	ESR	WBC	NEUTR	BAND	LYMPH	MONOC	EOSIN	BASOP	PLASM	ATYPL	GRANU	OTHER	ME	MY	PC	PB	AN	PI	MA	MI	HY	PL	BS	LE
F91396	27-JUL-92	9.2	30.1	4.71	19.5	64.0	30.6				677		5.0	1750		2900	350																		
F91396	16-DEC-97	10.3	33.6	4.95	20.9	67.9	30.8	0			332		9.6	3840	0	4416	480	768	0	0			0	0	0	0	0						2			
F91396	02-JAN-98	10.7	35.0	5.13	20.9	68.2	30.6	0			179		6.2	2852	0	2790	310	62	0	0			0	0	0	0	0						1			
F91396	16-JAN-98	9.9	31.8	4.73	21.0	67.3	31.2	0			385		7.6	4104	0	3040	228	228	0	0			0	0	0	0	0									
F91396	30-JAN-98	10.3	33.2	4.94	20.8	67.2	30.9	0			354		6.3	2583	0	2268	189	1260	0	0			0	0	0	0	0						1			
F91396	11-FEB-98	11.0	34.5	5.19	21.2	66.4	32.0	0			363		4.2	1764	0	1974	294	168	0	0			0	0	0	0	0						1			
	Comment: Ketamine + Atropine sedative used.																																		
F91396	12-FEB-98	9.0	28.9	4.27	21.0	67.6	31.1	0			268		7.8	6396	0	1170	156	78	0	0			0	0	0	0	0						1			

```
  Comment: Maternal blood sample.
F91396 19-FEB-98   8.6  26.7  4.03  21.4  66.3  32.3   0            406        3.0 |  1410       1410   120    30                          30 |             |  1          2
|
  Abnormal cell description: PLASMOCYTE
F91396 20-FEB-98   8.6  26.6  3.98  21.6  66.8  32.3   0            372        3.2 |  1088       1792   192   128                             |             |             1
|
F91396 26-FEB-98   9.2  30.2  4.50  20.6  67.1  30.7   0            313        5.4 |  3078       1836   432    54                             |             |             1
|
F91396 05-MAR-98   9.6  31.1  4.64  20.6  67.2  30.7   0            356        4.4 |  2596       1540   264                                   |             |
|
F91396 12-MAR-98   9.5  31.2  4.63  20.5  67.3  30.5   0            383        5.1 |  1581       2346   612   561                             |             |     1       1
|
F91396 13-MAR-98   9.2  30.6  4.56  20.2  67.2  30.1   0            388        5.2 |  1872       1924   312  1092                             |             |             1
|
F91396 19-MAR-98   8.4  27.3  4.07  20.6  67.2  30.7   0            354        5.4 |  3186     0 1890   162   162     0     0                 0 |  0  0  0  0 |             2
|
  Comment: Maternal sample
F91396 20-JAN-99   9.5  32.0  4.58  20.6  69.0  29.8                463        4.3 |  2451       1419   258   129    43                       |             |
|
  Comment: RBC Morphology- within normal limits Platelet Morphology- within
           normal limits WBC Morphology- See differential
F91396 02-MAY-00   7.8  26.0  3.79  20.5  68.0  30.2                442        5.6 |  3608       1499   333    56    56                       |             |
|
```

*** Blood Parasite Records *** (All 6 Records)

Tested	Parasite Type	Quantity	Other Description
16-DEC-97	Not Seen		
02-JAN-98	Not Seen		
16-JAN-98	Not Seen		
30-JAN-98	Not Seen		
11-FEB-98	Not Seen		
12-FEB-98	Not Seen		

*** Blood Chemistries *** (All 13 Records)

NOTE: We enter zero whenever labs report a result below the detectable limit for their analyzer.
NOTE: Some values have not been added to this report due to formating limitations.
Please see Other Reports > Blood Chemistry Reports for an Excel view of all possible results.

Animal	Tested	Lab	Na	K	Cl	CO2	IG	TP	Alb	Glo	A/G	Cal	PO4	PCO2	TBi	BUN	Glu	Crt	Alk	SGOT	SGPT	GGTP	Ldh	Chol	Tri	UA	Ph	Amy	Lip	CPK	T3	T4	Fe
F91396	27-JUL-92	PFS CL	148.0	6.3	119	19		5.6								10	51	0.5															
F91396	31-JUL-92	PFS CL	144.0	4.6	112	17		5.0								13	86	0.5															
F91396	30-NOV-94	PFS CL	145.0	3.7	111	25		7.6	3.1	4.5	0.689	9.7	4.7		0.40	28	65	0.6		37	36												
F91396	16-JAN-98	UW Hosp	145.0	4.0	108	25	12	6.1	2.7	3.4	0.794	8.4	4.5		0.40	14	51	0.4															
Comment: IRON, SERUM: 80 IRON BINDING CAPACITY: 453 TRANSFERRIN SATURATION: 18																																
F91396	30-JAN-98	UW Hosp	143.0	3.8	109	25	9	6.0	2.8	3.2	0.875	8.0	5.0		0.40	9	58	0.4															70
Comment: IRON BINDING CAPACITY: 433 TRANSFERRIN SATURATION: 16																																
F91396	11-FEB-98	UW Hosp	143.0	3.6	109	22	12	6.7	3.2	3.5	0.914	8.3	5.3		0.30	7	55	0.4															102
Comment: IRON BINDING CAPACITY (TOTAL): 437 TRANSFERRIN SATURATION: 23																																
F91396	12-FEB-98	UW Hosp	148.0	2.8	119	21	8	2.6	2.0	0.6	3.333	7.4	5.0		0.30	6	64	0.3															138
F91396	19-FEB-98	UW Hosp	145.0	4.3	108	26	11	5.9	2.5	3.4	0.735	8.2	5.2		0.20	8	50	0.4															89
Comment: iron binding capacity: 386 transferrin saturation: 23																																
F91396	20-FEB-98	UW Hosp	144.0	4.1	110	23	11	5.7	2.4	3.3	0.727	8.0	5.4		0.20	9	67	0.4															122
Comment: iron binding capacity: 387 transferrin saturation: 32																																
F91396	12-MAR-98	UW Hosp	148.0	3.1	116	14	18	4.0	2.7	1.3	2.077	8.1	6.4		0.40	9	20	0.3															
F91396	12-MAR-98	UW Hosp	144.0	4.4	108	22	14	6.2	2.6	3.6	0.722	8.3	5.3		0.40	8	39	0.3															98
F91396	13-MAR-98	UW Hosp	144.0	4.6	110	23	11	5.9	2.4	3.5	0.686	8.1	4.9		0.30	9	73	0.4															102
Comment: iron binding capacity: 429 transferrin saturation: 24																																

F91396 02-MAY-00 UW Hosp 147.0 3.9 112 5.7 1.6 4.1 0.390 7.6 4.7 0.20 8 99 0.6 138 34 17 57 100

*** No CSF Test Records ***

*** No Urinalysis Test Records ***

*** Snomed Reports *** (All IQs; All 29 Records)
(Please note that some test results are available only through MICRO and VIRUS.)

Prophylactic Treatment from 27-JUL-92 to 03-AUG-92:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. CLAVAMOX.

Clinical Procedure on 15-SEP-92:
SKIN OF CHEST. TATTOOING performed.

Prophylactic Treatment on 22-JUL-96:
ALOPECIA of ENTIRE BODY. PHYSICAL EXAMINATION performed. Ivermectin.
moderate, PLAQUE of ALL TEETH. NECROTIZING ULCERATIVE GINGIVITIS.
NOLVADENT.

Clinical Procedure on 26-MAR-97:
INJECTION SUBCUTANEOUS performed. Ivermectin.

Clinical Disorder on 15-SEP-97:
REPRODUCTIVE EXAM.
Dental Prophylaxis, Cleaning performed.
ADMINISTRATION OF MEDICATION, SUBCUTANEOUS performed. Ivermectin.
BLOOD COLLECTION performed.
SRV,STLV.

Clinical Disorder from 16-APR-98 to 26-APR-98:
DIARRHEA.
PROTOZOAL.
Additionally, FECAL COLLECTION FOR CULTURE & SENSITIVITY & PARASITOLOGY performed. GIARDIA.
Additionally, TRICHOMONAS.
For which was done: Bismuth Subsalicylate (Pepto Bismol).
Metronidazole (Flagyl).

Clinical Procedure on 25-AUG-98:
ULTRASOUND IMAGERY PROCEDURE performed.

Clinical Procedure from 13-DEC-98 to 14-DEC-98:
MULTIPLE SITES. INJURY DUE TO FIGHTING.
For which was done: Benzathine/Procaine penicillin G.
Ketoprofen (Ketofen).

Clinical Procedure from 20-JAN-99 to 26-JAN-99:
POSTPARTUM STATE.
The above is associated with PAIN.
For which was done: CBC AND BLOOD CHEMISTRY performed. Cephalexin (Keflex).
Acetaminophen (Tylenol).
Vitamin, injectable.

OXYTOCIN, CALPHOSAN, VIT. A,D,C,B.
Antibiotic.

Clinical Procedure on 01-FEB-99:
Ivermectin.

Clinical Procedure from 14-JUN-99 to 14-JUN-99:
Dental Prophylaxis, Cleaning performed. Ivermectin.

Clinical Procedure from 31-AUG-99 to 31-AUG-99:
PREPARTUM EXAM performed.

Clinical Procedure from 13-SEP-99 to 13-SEP-99:
POSTPARTUM EXAM performed.

Clinical Procedure on 08-DEC-99:
Dental Prophylaxis, Cleaning performed. Ivermectin.

Clinical Procedure on 05-APR-00:
PREPARTUM EXAM performed.

Clinical Procedure on 18-APR-00:
PREPARTUM EXAM performed.

Clinical Procedure on 02-MAY-00:
POSTPARTUM EXAM performed.

Clinical Disorder from 09-JUN-00 to 17-JUL-00:
severe DIARRHEA.
For which was done: ADMINISTRATION OF MEDICATION, ORAL performed.
Lactobacillus, Oral.
ADMINISTRATION OF MEDICATION, ORAL performed. Bismuth Subsalicylate (Pepto Bismol).
ADMINISTRATION OF MEDICATION, ORAL performed. Metronidazole (Flagyl).
SPECIAL DIET performed.
Rice and yogurt.
The above is followed by RECTAL MUCOUS MEMBRANE. SPECIMEN COLLECTION, MICROBIOLOGY, SWAB performed.
FECAL COLLECTION FOR PARASITOLOGY performed.
MICROBIAL SMEAR EXAMINATION performed.
The above is followed by ADMINISTRATION OF MEDICATION, ORAL performed.
Trimethoprim and Sulfamethoxazole.
ADMINISTRATION OF MEDICATION, ORAL performed. Metronidazole (Flagyl).
The above resulted in TREATMENT RESPONSE, GOOD.

Clinical Procedure from 18-JUL-00 to 18-JUL-00:
with TB test.
Dental Prophylaxis, Cleaning performed.
Additionally, DE-WORM performed. Ivermectin.
PHYSICAL EXAMINATION, COMPLETE performed.

Clinical Procedure on 25-SEP-00:
Dental Prophylaxis, Cleaning performed.

Experimental Procedure from 07-NOV-00 to 07-NOV-00:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine HCl.
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Atropine.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

Clinical Disorder from 23-NOV-00 to 04-DEC-00:
DEHISCENCE OF WOUND of SURGICAL SITE.
Following: SURGERY, EXPERIMENTAL performed.
For which was done: LUMBAR REGION. DEBRIDEMENT performed. Sodium chloride.
The above is followed by LUMBAR REGION. RESUTURE OF WOUND DEHISCENCE performed.
Additionally, ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Benzathine/Procaine penicillin G.
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketoprofen (Ketofen).
ADMINISTRATION OF MEDICATION, ORAL performed. Cephalexin (Keflex).
The above is followed by DEHISCENCE OF WOUND of SURGICAL SITE.
For which was done: LUMBAR REGION. DEBRIDEMENT performed.
LUMBAR REGION. RESUTURE OF WOUND DEHISCENCE performed.
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketoprofen (Ketofen).
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Buprenorphine (Buprenex).
ADMINISTRATION OF MEDICATION, ORAL performed. Ketoprofen (Ketofen).
ROUTINE MONITORING performed.

Experimental Procedure from 15-DEC-00 to 15-DEC-00:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

Clinical Procedure from 26-DEC-00 to 26-DEC-00:
with TB test.
Dental Prophylaxis, Cleaning performed.
Additionally, DE-WORM performed. Ivermectin.
PHYSICAL EXAMINATION, COMPLETE performed.

Experimental Procedure from 12-JAN-01 to 12-JAN-01:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

Experimental Procedure from 09-FEB-01 to 09-FEB-01:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL

performed.
DEXA, BONE SCAN performed.

Experimental Procedure from 08-MAR-01 to 08-MAR-01:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

Experimental Procedure from 05-APR-01 to 05-APR-01:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

Experimental Procedure from 10-MAY-01 to 10-MAY-01:
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Ketamine/Xylazine Combination.
The above is followed by LUMBAR VERTEBRA. DIAGNOSTIC RADIOGRAPHY, COMBINED AP AND LATERAL performed.
DEXA, BONE SCAN performed.

*** Microbiology Reports *** (All 7 Records)
27-JUL-92 0 92M-0948 PFS Clinical Lab
Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
-- Bacteriology --
137X CAMPYLOBACTER JEJUNI / COLI GROUP: 4+ many
1652 SHIGELLA FLEXNERI (GROUP B): 2+ few

Amikacin	sensitive
Ampicillin	sensitive
Carbenicillin [CARB]	sensitive
Cefoxitin	sensitive
Cephalothin	sensitive
Chloramphenicol	sensitive
Erythromycin [ERM]	resistant
Gentamicin [GM]	sensitive
Kanamycin [KAN]	sensitive
Metronidazole	sensitive
Moxalactam	sensitive
Penicillin	resistant
Sulfa Trimethoprim - SXT	sensitive
Tetracycline	resistant

16-APR-98 0 98U-0261 University of Washington Hospital Lab
Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
-- Parasitology --
4415 GIARDIA, NOS: present
4432 TRICHOMONAS, NOS: present

30-APR-98 0 98U-0108 Seattle Clinical Lab

Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
Normal flora: present

02-MAY-00 0 University of Washington Hospital Lab
Type: secretion
Site: vagina
How-taken: direct swab
Purpose: diagnostic
-- Direct Smear --
- Visible organisms -
Gram negative bacilli: 4+ many
4+ Lactose fermenting gram negative rods
No cell matrix.
-- Bacteriology --
252X STREPTOCOCCUS GROUP D, ENTEROCOCCUS, NOS: 4+ many

16-JUN-00 0 Dr. Marilyn Roberts
Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
-- Bacteriology --
1466 CLOSTRIDIUM PERFRINGENS: present
2440 STAPHYLOCOCCUS, NOS: 4+ many

16-JUN-00 10 Seattle Clinical Lab
Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
-- Parasitology --
4432 TRICHOMONAS, NOS: present
4482 BALANTIDIUM COLI: 1+ rare

19-JUN-00 0 Dr. Marilyn Roberts
Type: fecal / enteric
Site: rectum
How-taken: direct swab
Purpose: diagnostic
-- Bacteriology --
1466 CLOSTRIDIUM PERFRINGENS: present
2547 ALPHA HEMOLYTIC STREPTOCOCCUS, NOS: 4+ many

*** Virology Test Results *** (All 55 Records)
SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 2-OCT-92).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: negative by Elisa Test of plasma (Southwest Foundation, 12-OCT-92).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 19-OCT-92).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 19-OCT-92).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 19-JAN-93).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 19-JAN-93).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 14-JUN-93).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 14-JUN-93).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 19-NOV-93).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 19-NOV-93).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 10-MAY-94).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 30-NOV-94).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 30-NOV-94).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 1-AUG-95).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of whole blood (PFS Virology Laboratory, 2-AUG-95).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 17-JAN-96).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (PFS Virology Laboratory, 14-MAR-96).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of serum (SRV Seattle Lab, 15-SEP-97).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of serum (SRV Seattle Lab, 15-SEP-97).

STLV-I antibody test: negative by Elisa Test of serum (VRL (Virus Reference Lab), 29-SEP-97).

SRV-2 (Type D / Washington) virus test: negative by Raji Cell Culture of serum (SRV Seattle Lab, 6-NOV-97).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of serum (SRV Seattle Lab, 6-NOV-97).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (NIH B Virus Resource Lab, 20-JAN-98).
Test comment: >1:5000 CONFIRMED BY WESTERN BLOT

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral Cell Culture of buccal swab (NIH B Virus Resource Lab, 20-JAN-98).

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral Cell Culture of right eye swab (NIH B Virus Resource Lab, 20-JAN-98).

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral

Cell Culture of left eye swab (NIH B Virus Resource Lab, 20-JAN-98).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (NIH B Virus Resource Lab, 20-JAN-98).
Test comment: CONFIRMED BY WESTERN BLOT
Numerical results:
>1:5000

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (NIH B Virus Resource Lab, 9-FEB-98).
Numerical results:
>1:5000

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 1-APR-98).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 1-APR-98).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 6-OCT-98).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 6-OCT-98).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (UW Seattle Diagnostic Lab, 6-OCT-98).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 18-JAN-99).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 18-JAN-99).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (UW Seattle Diagnostic Lab, 18-JAN-99).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 1-FEB-99).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 1-FEB-99).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (UW Seattle Diagnostic Lab, 1-FEB-99).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 14-JUN-99).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 14-JUN-99).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 25-OCT-99).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 25-OCT-99).

STLV-I antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 25-OCT-99).
Test comment: VIFE

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 2-MAY-00).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 2-MAY-00).

STLV-I antibody test: negative by Elisa Test of plasma (Animal Medicine / Thouless, 2-MAY-00).

STLV-I antibody test: negative by Elisa Test of plasma (Animal Medicine / Thouless, 18-JUL-00).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (Animal Medicine / Thouless, 18-JUL-00).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (Animal Medicine / Thouless, 18-JUL-00).

STLV-I antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 25-SEP-00).

STLV-I antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 26-DEC-00).

SRV-2 (Type D / Washington) antibody test: negative by Elisa Test of plasma (UW Seattle Diagnostic Lab, 26-DEC-00).

SRV-2 (Type D / Washington) viral DNA test: negative by PCR (Polymerase Chain Reaction Assay) of lymphocytes (UW Seattle Diagnostic Lab, 26-DEC-00).

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral Cell Culture of buccal swab (NIH B Virus Resource Lab, 8-MAR-01).

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral Cell Culture of right eye swab (NIH B Virus Resource Lab, 8-MAR-01).

CHV-1 (B virus), Cercopithecine herpesvirus 1 virus test: negative by Viral Cell Culture of left eye swab (NIH B Virus Resource Lab, 8-MAR-01).

CHV-1 (B virus), Cercopithecine herpesvirus 1 antibody test: positive by Elisa Test of serum (NIH B Virus Resource Lab, 8-MAR-01).
Test comment: Confirmed by Western Blot.
Numerical results:
>1:5000
Summary for animal:

*** Surgery Reports *** (All 7 Records)
11-FEB-98: Experimental Surgery Infant Primate Research Laboratory.
CATHETER.
MATERNAL/FETAL.
Surgeon: Unknown Missing or unknown code
Coded-by: LDR

11-FEB-98: Major Experimental Surgery Miscellaneous Seattle Colony.
General anesthesia: Halothane
Route: Cuffed Intratracheal Tube
Fluid administration: Lactated Ringer's Solution
Investigator: Sackett, Gene P. Program: 46 Project: 1
Surgeon: Weyhrich P.C. Staff
Coded-by: LDR
MATERNAL/FETAL CATHETER.

13-FEB-98: Experimental Surgery Infant Primate Research Laboratory.
CAESAREAN SECTION performed.
Surgeon: Unknown Missing or unknown code
Coded-by: LDR

01-APR-98: Experimental Surgery Infant Primate Research Laboratory.
REMOVAL OF CATHETER performed.
Surgeon: Unknown Missing or unknown code
Coded-by: TW

01-APR-98: Minor Experimental Surgery Cath./Shunt Removal Seattle Colony.
General anesthesia: Isoflurane
Route: Cuffed Intratracheal Tube
Investigator: Sackett, Gene P. Program: 46 Project: 1
Surgeon: Weyhrich/Nosbisch P.C. Staff
CATH. REMOVAL (COLONY).

09-MAY-00: Experimental Surgery Seattle Colony.
POSTPARTUM EXAM performed.
Surgeon: Unknown Missing or unknown code
Coded-by: mj

16-NOV-00: Minor Experimental Surgery Orthopedic Seattle Colony.
Vertebral body. INJECTION performed.
L-3 and L-5.
For which was done: ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed.
Ketoprofen (Ketofen).
ADMINISTRATION OF MEDICATION, INTRAMUSCULAR performed. Oxymorphone.
General anesthesia: CRI of Fentanyl
Route: Cuffed Intratracheal Tube
Fluid administration: Lactated Ringer's Solution
Investigator: Morton, William R. Program: 88 Project: 5
Surgeon: Astley P.C. Staff
Coded-by: MJ

*** No Psychological Well-being Program Records ***

*** No Daily Observation Records ***

***** End of Report for F91396 *****

General anesthesia: CRI of Fentanyl
Route: Cuffed Intratracheal Tube
Fluid administration: Lactated Ringer's Solution
Investigator: Morton, William R. Program: 88 Project: 5
Surgeon: Astley P.C. Staff
Coded-by: MJ

***** End of Report for F91396 *****