copy of original letter

October 16, 2002

Rebecca Beatty
University of California Los Angeles
Record Management and Information Practices
10920 Wilshire Blvd., Suite 500
Los Angeles, California 90024

Dear Ms. Beatty:

I am writing to request information on a vervet in one of the laboratories at UCLA. Under the California Public Records Act, the documentation I am requesting is available to the public.

The vervet in question is a female, #1991-016. I would like to know whether or not this monkey is still alive. If alive, is she caged alone or with other vervets? What is her medical status? And for what kind of research is she being used? What are the future plans for her? If she is dead, what were the conditions surrounding her death?

As this information is also considered public record under the California Freedom of Information Act, I would really appreciate hearing from you as soon as possible.

Thanks so much for your time.

Sincerely,

Joy S. Kennedy

Joy S. Kennedy
[redacted]

(SASE enclosed for your convenience)

(11.5.02)
Hi - I've now sent 3 copies of this letter (with dates changed each time) to UCLA. Enclosed is a copy of their "reply" thus far - received 11.4.02. I noticed it's signed by someone else other than who I sent it to, and that there's a phone number, also. Will let you know when I hear more... I will continue to pursue the matter until I get some satisfactory answers. As a last resort, I'll call.... any ideas re: what I might ask when I call, other than what I asked in the letter? Thanks! Hope to hear from you!

Joy Kennedy
(address above)
pager (digital) [redacted]
e-mail address: [redacted]

e: Primate Freedom
Tag info

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LOS ANGELES, CALIFORNIA 90024-6302

copy of "reply" thus far - received 11.4.02

October 28, 2002

Ms. Joy S. Kennedy
[redacted]

Dear Ms. Kennedy:

I am writing in response to your October 16, 2002 letter requesting information pertaining to a vervet (number 1991-016).

this is a crock!

We are in the process of searching for responsive documents which would be disclosable pursuant to the California Public Records Act. We will notify you in writing when the records are ready to be released.

Please call me at (310) 794-8960 should you have any questions.

Sincerely,

Linda Arquieta
Information Practices Office

cc: Assistant Vice-Chancellor Lawrence Lokman

wonder why they'd send him a copy?

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2nd letter (received 11.13.02) You can tell they're already tired of hearing from me (too bad....) If I don't hear something by the end of next week, I'll call over Thanksgiving break - Joy Kennedy

November 6, 2002

Ms. Joy S. Kennedy

[redacted]

Dear Ms. Kennedy:

I am writing in response to your October 24th and October 31st, 2002 letters requesting information pertaining to a vervet (number 1991-016).

A response letter was sent to you on October 28, 2002 acknowledging your original request letter. We replied to your correspondence to the address you listed on your letter. If you would like to provide us with a phone number in order to be able to reach you regarding your request, you may do so either by mail or by calling me at (310) 794-8688.

We are in the process of searching for responsive documents which would be disclosable pursuant to the California Public Records Act. We will notify you in writing when the records are ready to be released.

Please call me at (310) 794-8688 should you have any questions.

Sincerely,

Rebecca Beatty
Information Practices Officer

cc: Assistant Vice Chancellor Lawrence Lokman

Also, this is the original person I've sent letters to. The 1st reply came from someone else - (I sent you copies of 1st reply...)

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LOS ANGELES, CALIFORNIA 90024-6302

(received 11-25-02)

November 15, 2002

Ms. Joy S. Kennedy
[redacted]

Dear Ms. Kennedy:

I am writing in response to your October 24th and October 31st, 2002 letters requesting information pertaining to a vervet (number 1991-016).

We are providing the following information in response to your inquiry. Vervet number 1991-016 is living in a large stable social group with 24 other animals, including two sisters and other members of her extended matriline. She is healthy with no problems noted during the annual veterinary exam or daily health checks. Her behavior is being observed for a NIMH study, "Behavioral genetics of impulsivity". The future plans for her are to remain in her social group.

Please call me at (310) 794-8688 should you have any questions.

Sincerely,

Rebecca Beatty
Information Practices Officer

cc: Assistant Vice Chancellor Lawrence Lokman

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LOS ANGELES, CALIFORNIA 90024-6302

March 25, 2003

Ms. Joy S. Kennedy
[redacted]

Dear Ms. Kennedy:

I am writing in response to your January 30, 2003 letter requesting information pertaining to vervet number 1991-016.

Thank you for your payment in the amount of $2.20. Enclosed are the 22 responsive documents.

Sincerely,

Linda Arquieta
Information Practices Office

cc: Assistant Vice Chancellor Lawrence Lokman

Response to Joy Kennedy's request for further information on female vervet 1991-016

1. Last year's veterinary exams were performed by Dr. Janusz Jawien. He did not provide a written report. A copy of this year's veterinary examination is attached.
2-3. All health-related information on this female from our colony record data base is attached.
4. This female is a subject in my research project, Behavioral Genetics of Impulsivity. The UCLA approved protocol is attached.
5. Correspondence with the UCLA Animal Research Committee on this protocol is incorporated into the protocol, as indicated.

B11-Y

VERVET RESEARCH COLONY, PHYSICAL EXAM

___REQUIRES VET FOLLOW-UP

TATTOO # 1991-016 DATE 1/15/03 SPECIES_____

WEIGHT_____KG MALE FEMALE PHYSICAL: ENTRY EXIT ANNUAL

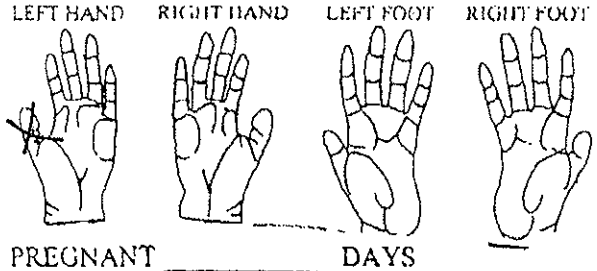
TEMPERATURE 98.9 BODY CONDITION SCORE: 1 2 3 4 5 6 7 8 9 10
Thin Normal Obese

PULSE 160

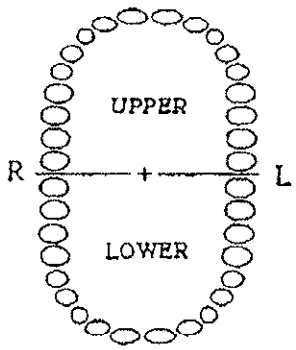
RESPIRATION 36

Normal	Abnormal	
[X]	[ ]	EENT
[ ]	[ ]	HEAD
[ ]	[ ]	HEART/LUNGS
[ ]	[ ]	ABDOMEN
[ ]	[ ]	EXTREMITIES
[ ]	[ ]	UROGENITAL
[ ]	[X]	COAT/TAIL OLD SCARS TAIL, MISSING 1/4 TAIL -INJURY RESOLVED
[ ]	[ ]	INTEGUMENT
[X]	[ ]	LYMPH NODES

LEFT HAND RIGHT HAND LEFT FOOT RIGHT FOOT



DENTITION
(Grade 0 - 5) Tartar____ Gingivitis____
"O" over defective teeth, "X" over missing



PREGNANT _____ DAYS_____

NAILS TRIMMED _____

NEEDS DENTAL _____

LABORATORY WORKUP (Circle all that apply)

CBC / CHEM / SRV / MACAQUE AB / FECAL CUL / OP / OTHER_____

COMMENTS_____

PERFORMED BY _____ DVM

VRC Animal Report

Wednesday, February 12, 2003

AnimalID:	1991-016	**Sex:**	F
Enclosure Name:	B11-Y	**IDMarks:**	Yellow; "Y"
Tattoo:	9116	**Date of Birth:**	15-Jun-1991
Mother's ID:	1980-001	**Date of Death:**	

MEDICAL RECORDS

MedDate	DiagCode	Quant	Description
10-Jul-1991	TB		NEGATIVE
27-Mar-1992	TT		
29-Apr-1993	TB		NEGATIVE
29-Apr-1993	BLOOD		
05-Aug-1993	BLOOD		
09-Sep-1993	BLOOD		
20-Oct-1993	BLOOD		
20-Oct-1993	TB		NEGATIVE
01-Dec-1993	BLOOD		
28-Jan-1994	BLOOD		
15-Apr-1994	TB		NEGATIVE
15-Apr-1994	GLUCOSE	54	
15-Apr-1994	BLOOD		
26-May-1994	ULTRASOUN		ULTRASOUND PERFORMED BY DR. TARANTAL BIPARIETAL DIAMETER = 44 PREDICTED GESTATIONAL AGE DETERMINED BY COMPARISON WITH M. FASICULARIS = 144-150 DAYS
16-Jun-1994	GAVE BIRTH		
23-Jun-1994	CSF &BLOOD		
23-Jun-1994	GLUCOSE	86	
04-Aug-1994	BLOOD		
04-Aug-1994	GLUCOSE	94	TWO READINGS WERE TAKEN FOR COMPARISON SECOND READING WAS 73.0
22-Sep-1994	BLOOD		
18-Nov-1994	CSF &BLOOD		
21-Apr-1995	CSF &BLOOD		POSSIBLY PREGNANT
25-Jul-1995	GAVE BIRTH		
25-Aug-1995	CSF &BLOOD		
25-Aug-1995	GLUCOSE	84	
03-Nov-1995	CSF &BLOOD		
03-Nov-1995	GLUCOSE	75	
25-Mar-1996	FECAL EXAM		NEGATIVE
19-Jun-1996	GAVE BIRTH		
03-Dec-1996	TT		

03-Dec-1996	TB		NEGATIVE
19-Apr-1997	GAVE BIRTH		
09-Jul-1997	CSF &BLOOD		
09-Jul-1997	TB		NEGATIVE
18-Sep-1997	DNA-SWF		DNA SHIPPED TO [redacted] AT SOUTHWEST FOUNDATION FOR DNA EXTRACTION
19-Sep-1997	BLOOD		for DNA analysis
13-Oct-1997	DEWORMED		RECEIVED 15MG/KG PANACUR(FEBENDAZOLE)
14-Oct-1997	DEWORMED		RECEIVED 15MG/KG FEBENDAZOLE
15-Oct-1997	DEWORMED		RECEIVED 15MG/KG PANACUR (FEBENDAZOLE)
16-Dec-1997	TT		
24-Apr-1998	GAVE BIRTH		
03-Feb-1999	CSF &BLOOD		
03-Feb-1999	TB		NEGATIVE
03-Feb-1999	TT		
03-Feb-1999	DNA-SWF		BLOOD SAMPLE SHIPPED TO [redacted] AT SOUTHWEST FOUNDATION FOR DNA EXTRACTION
17-Mar-2000	CSF		
17-Mar-2000	TB		NEGATIVE
17-Mar-2000	TT		
18-May-2000	FECAL EXAM		Negative for parasites by direct smear and flotation.
30-Aug-2000	WOUNDS1		Has wound behind left shoulder
20-Sep-2000	WOUNDS1		Has swollen right eye.
22-Jan-2001	DNA-UCLA		
22-Jan-2001	BLOOD		
22-Jan-2001	TB		Negative
10-Dec-2001	HEALTH		Annual health check by Dr. Jawien.
10-Dec-2001	GLUCOSE	50	Annual Roundup B11
10-Dec-2001	CSF		Annual roundup B11, frozen at VRC to be assayed by John Mann
10-Dec-2001	DNA-UCLA		Annual roundup B11, yellow-top (citrate)
10-Dec-2001	DNA-VRC		Roundup B11, yellow-top. 2 Omni-vials in VRC freezer, box WBS-003
10-Dec-2001	TB		Negative

WEIGHT AND LENGTH RECORDS

Date	Weight (kg)	Length (cm)
27-Mar-1992	1.60	27.0
27-Aug-1992	2.00	31.0
03-Nov-1992	2.40	29.5
06-May-1993	2.68	31.0
05-Aug-1993	3.08	33.0
09-Sep-1993	3.12	33.0
20-Oct-1993	3.37	33.0
01-Dec-1993	3.57	33.0
28-Jan-1994	3.80	33.0
15-Apr-1994	4.81	33.0
23-Jun-1994	4.35	35.0

04-Aug-1994	4.20	34.0
22-Sep-1994	4.24	34.0
18-Nov-1994	4.58	35.5
13-Jan-1995	2.68	31.0
21-Apr-1995	4.87	36.0
25-Aug-1995	4.70	36.0
03-Nov-1995	5.23	35.5
03-Dec-1996	5.44	35.5
09-Jul-1997	5.83	
19-Sep-1997	5.32	
03-Feb-1999	5.82	45.6
17-Mar-2000	5.86	44.7
22-Jan-2001	5.60	45.2
10-Dec-2001	6.10	45.4
	13.416	17.87in

University of California, Los Angeles
Chancellor's Animal Research Committee (ARC)

Renewal Application

General Information	
Title:	Behavioral Genetics of Impulsivity
Protocol #:	1999-162-11
PI:	Lynn Fairbanks, Ph.D.
Status:	APPROVED
Approval Period:	9/27/2002-9/26/2003
Received Date:	8/9/2002
Type:	Renewal
Species:	50 Vervet Monkey, 675 Vervet Monkey
Create Date:	7/22/2002 1:53:21 PM
Created By:	Lynn Fairbanks
Owner:	Lynn Fairbanks

Updated Sections
Animal Care
Contacts
Experimental Design
General Literature Search
Locations
Non-Surgical Procedures
Pain Category
Pain Category Assignments
Pain Literature Search
Personnel
PI Assurance
Pre-Review
Rationale
Renewal Summary
Research Summary
Species Euthanasia
Species Medication
Tissue Collection

Renewal

1. Please indicate whether any adverse effect or unanticipated problems have been experienced, including higher than anticipated mortality/morbidity regardless of the cause. If so, please provide an explanation of how these events/problems were resolved.

No

2. To assist the ARC in documenting scientific progress arising from use of animals under this protocol, please provide ONE of the following:

- ○ Citation(s) of presentations or articles resulting from this protocol (either accepted or submitted). Please include an abstract.
- ○ A brief (1-2 sentence) update regarding progress made toward achieving the scientific objective(s) of this protocol.
- ◉ A copy of the most recent annual progress report submitted to the funding agency.

If the scientific progress documentation is in a text format, please paste (or type) it here. Otherwise, you will need to submit it to the ARC as a hard copy.

a. Specific Aims
The specific aims of this project are to: 1) Assess the relative contribution of genetic and environmental factors to variation in impulsivity at different life stages; 2) Determine the contribution of specific early experiences (maternal style, family social status, peer relationships) to variation in impulsivity; and,
3) Evaluate the role of monoaminergic neurotransmitter systems in mediating genetic influences on impulsivity. These aims have not been modified from the original proposal.

b. Studies and Results
Data collection is underway in all domains of this longitudinal study, including quantitative assessment of early experience with the mother, family social status, home group behavior, and assessment of impulsivity in response to social and nonsocial challenges at key stages of development.
In the past year, we have completed a cross-sectional analysis using variance component methods to assess genetic and maternal environmental contributions to variation in social impulsivity in 352 adult males and females (Specific Aim

1). The genetic component was estimated using the matrix of degree of relatedness between all subject pairs from the colony pedigree, and the shared maternal effects were modeled by incorporating a unique environmental value for pairs that share the same mother. The results, which have been prepared for publication, indicated that there were significant genetic and maternal environmental contributions to individual differences in social impulsivity (Table 1). The Approach Subscale of the Social Impulsivity Index, which involves rushing over and engaging a stranger at close quarters, was significantly influenced by both genetic and maternal environmental factors. The Aggression Subscale of the Social Impulsivity Index was strongly influenced by genetic factors, but not by maternal environment.

Table 1. Genetic (h2) and Maternal Environmental (m2) Effects on Impulsivity (N=352)

Index	h2 (S.D.)	p value	m2 (S.D.)	p value
Social Impulsivity Index	0.35 (0.13)	p=0.0023	0.16 (0.07)	p=0.01
Approach subscale	0.26 (0.11)	p=0.003	0.16 (0.08)	p=0.01
Aggression subscale	0.56 (0.15)	p=0.000001		

Progress has also been made in Aim 3, to identify neurobiological mediators of behavioral differences in impulsivity. The assays have been completed for metabolites of serotonin (5-HIAA), dopamine (HVA) and norepinephrine (MHPG) from last winter's samples. All three metabolites in this new data set show strong genetic heritability (5-HIAA, h2 = 0.70 (0.16), p<.000006; HVA, h2 = 0.66 (0.16), p<.000002; MHPG, h2 = 0.60 (0.14), p<.0000015), with no significant maternal environmental effects. Our statistical geneticist, Dr. Julia Bailey is working with our colleagues at Southwest Foundation for Biomedical Research to determine the genetic covariance among the three monoamines. The pattern of covariance among these interrelated systems will help us to target which candidate genes are most likely to be influencing monoamine metabolite levels.
Work has also begun on the second part of aim 3, to identify genetic polymorphisms at loci in serotonergic and dopaminergic pathways. Because of promising results with rhesus monkeys in other laboratories, the first candidate gene selected for screening was the serotonin transporter. Unfortunately, we did not find any variation in this gene in a test sample of 10 unrelated animals. Work is currently in progress to identify polymorphisms in the dopamine transporter and the dopamine receptor (DRD4).

c. Significance
This is the first report of significant maternal effects, within the normal range of variation in mother-infant relationships, on adult personality traits for any nonhuman primate species. Human studies using twin or adoptions designs have found remarkably little evidence for shared family environmental influences on personality, particularly in adulthood. This is in contrast to experimental evidence from animal studies, and strong beliefs by developmental psychologists to the contrary. We proposed that the vervet monkey model used here would help to resolve some of the discrepancies between these different approaches. The vervet breeding system and lack of involvement of fathers in the development of their offspring allowed us to separate maternal environmental influences from maternal and paternal genetic influences in normally reared animals using the extended pedigree, thus avoiding potential biases introduced by twin and adoption designs. Our objective, quantitative measures of impulsivity also allowed us to avoid contrast effects and other problems of self-report and subjective rating scales. The promise of this approach is beginning to be felt in the results of the cross-sectional analyses completed in the first year of funding. As expected, we found significant genetic contributions to all aspects of our measure of social impulsivity, but our quantitative genetics approach also identified a significant contribution of maternal environment on adult variation in social impulsivity.
Interestingly, the maternal influence was found for the approach component of the scale, which involves rushing over and engaging a stranger at close quarters, and was absent for the aggressiveness component.

d. Plans
Our plans for the coming year involve continuation of data collection for the

longitudinal assessments in Specific Aim 2. The analysis described above modeled maternal influences by using a matrix identifying dyads with the same mother. As our longitudinal database grows, we plan to include quantitative measures of maternal style experienced in infancy for each subject, thus allowing us to specify the source of maternal influences more precisely.
We will look for genetic polymorphisms in dopamine transporter and receptor genes (DAT and DRD2) to use in quantitative linkage analyses with our behavioral and neurobiological measures. The high heritabilities that we found for the monoamine metabolites, combined with the Vervet Research Center pedigree, form a strong basis for finding linkage to the proposed candidate genes.
We currently have a pending proposal, with Dr. Nelson Freimer of the UCLA Center for Neurobehavioral Genetics, to use the Vervet Reseach Colony pedigree to construct a map of the vervet genome. A vervet marker-to-marker genetic map, which could be available in two years, would add enormously to the value of the data from the longitudinal study of social impulsivity. With a modest addition of funds for more extensive genotyping, any of the behavioral and neurobiological measures currently being collected that show significant heritabilities of 0.30 or higher could be included in a genome wide linkage analysis. This would allow expansion of the scope of the current project beyond the monoamine neurotransmitter systems under consideration, and provide the opportunity to identify new genes and physiological systems contributing to variation in impulsivity and other dimensions of temperament relevant to vulnerability for psychopathology.

Research Summary

Your answers to the questions on this page determine the other sections needed to be filled out.

1. What is the Title of the Project?

Behavioral Genetics of Impulsivity

2. What is your Recharge ID number (to cover copy costs)?

NP7M

3. Check all that apply:

- ☐ Tumor Formation
- ☐ Chronic Disease
- ☑ Tissue Collection
- ☐ Antibody/Ascites Production
- ☐ Surgical Procedures
- ☑ Non Surgical Procedures
- ☐ Gas Anesthetic Agent(s)
- ☐ rDNA, Chemical or Biohazardous Agents
- ☐ Radioisotopes
- ☐ Videotaping/Photography
- ☐ Prolonged Physical Restraint
- ☐ Genetically Modified Animals
- ☐ Tissue Sharing

4. Will the research be conducted exclusively on tissue received from another investigator?

No

If yes, do your funding sources require an ARC approved protocol?

No

5. Check all that apply:

- ☐ Experiments done entirely at another institution
- ☑ Experiments done entirely at VAGLAHS
- ☐ Program Project/Training Grant
- ☐ Breeding Colony: #

NOTE: If you will be breeding animals for this protocol and do not already have an approved breeding protocol on file with the ARC, you must submit an Application to Establish and/or Maintain a Breeding Colony at this time. Check the box above but leave the "Breeding Colony Number" field above empty. The ARC Staff will update the Breeding Colony Number following the submission of a breeding colony application.

6. If you are seeking approval for a training grant, list all individual projects supported by the program project or training grant, including the principal investigators' names and their current ARC approval numbers. If no animal research is currently being supported by the overall grant, please assure the Committee that, should an investigator of a project covered by the overall grant initiate research involving animals, ARC approval will be obtained prior to the distribution of funds.

Personnel

There can be only one Principal Investigator per protocol. To edit a person's contact information or add a new person to our system, click on the People tab above.

Please note that prior to the submission of an amendment to add personnel, please ensure that these individuals have completed all applicable animal use certification requirements and have a Medical History Questionnaire (MHQ) on file with the Occupation Health Facility (OHF). If you are only requesting the removal of personnel, please email the ARC staff (arc@oprs.ucla.edu). An amendment application is NOT required if you are only removing personnel.

Principal Investigator

Lynn A. Fairbanks, Ph.D.

Email:	[redacted]	**UID:**	001244101
Phone:	50782	**Degree:**	Ph.D.
Fax:	50705	**Dept:**	PSYCHIATRY/BIOBEHAVIORAL SCI
Status:	Faculty		

What role will this person be performing in this protocol?

Principal Investigator

Which species will this person handle in this protocol?

Vervet Monkey, Non-Human Primate (other)

Will this person handle animal tissue in this protocol?

Yes

Will this person be involved with Survival Surgery Procedures?

No

Will this person handle radioactive materials or radioactive animals?

No

Please provide a brief account of the person's qualifications and experience with the animal model(s) and procedures involved in this protocol as required by federal regulations. In addition, please list the duties that this person will perform related to this protocol.

Thirty years experience conducting behavioral studies of nonhuman primates; has been directing and participating in research with the vervet monkeys from

vervet monkeys in captivity and in the field. Experienced in animal capture and handling, ketamine injections and blood sample collection.

Personnel

[redacted]

Email:	
Phone:	[redacted]
Fax:	
Status:	

UID:	601073549
Degree:	Ph.D
Dept:	PSYCHIATRY/BIOBEHAVIORAL SCI

What role will this person be performing in this protocol?

Personnel

Which species will this person handle in this protocol?

Vervet Monkey, Non-Human Primate (other)

Will this person handle animal tissue in this protocol?

Yes

Will this person be involved with Survival Surgery Procedures?

No

Will this person handle radioactive materials or radioactive animals?

No

Please provide a brief account of the person's qualifications and experience with the animal model(s) and procedures involved in this protocol as required by federal regulations. In addition, please list the duties that this person will perform related to this protocol.

Experience in behavior of captive vervet monkeys since 1981. Expert in all of the proposed behavioral data collection protocols. Twenty years experience in animal capture, handling and ketamine injections. Extensive familiarity with individual animals at the VRC. Trained in blood sample collection.

Personnel

[redacted]

Email:	[redacted]
Phone:	[redacted]
Fax:	
Status:	Staff

UID:	202674740
Degree:	B.A.
Dept:	Psychiatry

What role will this person be performing in this protocol?

Personnel

Which species will this person handle in this protocol?

Vervet Monkey

Will this person handle animal tissue in this protocol?

Yes

Will this person be involved with Survival Surgery Procedures?

No

Will this person handle radioactive materials or radioactive animals?

No

Please provide a brief account of the person's qualifications and experience with the animal model(s) and procedures involved in this protocol as required by federal regulations. In addition, please list the duties that this person will perform related to this protocol.

Danielle has had 3 years of experience doing behavioral observations of nonhuman primates in captivity and in the field. She has been trained as an animal keeper at the Los Angeles Zoo, and is experienced in animal handling

and blood collection and processing at the Vervet Research Center.

Personnel

[redacted]

Email:	[redacted]
Phone:	
Fax:	
Status:	

UID:	002606926
Degree:	B.A.
Dept:	NEUROPSYCHIATRIC INSTITUTE

What role will this person be performing in this protocol?

Personnel

Which species will this person handle in this protocol?

Vervet Monkey, Non-Human Primate (other)

Will this person handle animal tissue in this protocol?

No

Will this person be involved with Survival Surgery Procedures?

No

Will this person handle radioactive materials or radioactive animals?

No

Please provide a brief account of the person's qualifications and experience with the animal model(s) and procedures involved in this protocol as required by federal regulations. In addition, please list the duties that this person will perform related to this protocol.

Three years experience at the VRC in the behavior of vervet monkeys. Trained to collect behavioral data for home group assessments and challenge tests. Previous training in exotic animal handling. Trained to assist in animal capture, handling and ketamine injections.

Personnel

[redacted]

Email:	
Phone:	[redacted]
Fax:	
Status:	

UID:	502619790
Degree:	
Dept:	PSYCHIATRY/BIOBEHAVIORAL SCI

What role will this person be performing in this protocol?

Personnel

Which species will this person handle in this protocol?

Vervet Monkey, Non-Human Primate (other)

Will this person handle animal tissue in this protocol?

Yes

Will this person be involved with Survival Surgery Procedures?

No

Will this person handle radioactive materials or radioactive animals?

No

Please provide a brief account of the person's qualifications and experience with the animal model(s) and procedures involved in this protocol as required by federal regulations. In addition, please list the duties that this person will perform related to this protocol.

Trained as a veterinary assistant in 1982 at the Yale University St. Kitts Biomedical Foundation. Chief veterinary technician at the VRC since 1987. Twenty years of experience in handling, health assessment, blood and cerebrospinal fluid collection for vervet monkeys. Responsible for training

blood sample collection.

Contacts

Name:	Lynn Fairbanks
Contact Type:	Emergency, Administrative
Home Phone:	310 441-1244
Mobile Phone:	
Email:	LFairbanks@mednet.ucla.edu

Funding

1. Funding Types (Check All That Apply):

- ☐ Department
- ☑ Extramural
- ☐ UCLA Academic Senate
- ☐ Gift
- ☐ Other:

Proposals

List all funding agencies to which this animal protocol has been or will be submitted for consideration. Include all pending applications.

For each grant/proposal submitted to a funding agency, submit a copy of the grant proposal. If the agency is not listed, please contact the **Office of Contracts and Grants.** Please note that the National Institutes of Health may be found by typing in the keyword "NIH" when searching for an Agency Code.

Agency Name:	NIH/MISCELLANEOUS AGENCIES & DEPARTMENTS
Agency Code:	000008
PI of Proposal/Award:	Lynn Fairbanks
Proposal/Award Title:	Behavioral Genetics of Impulsivity
Proposal/Award Number:	1 R01 MH61852:01A1

Rationale

1. Provide a non-technical summary of the overall objectives of the study.

The aims of this project are to use a nonhuman primate model, the vervet monkey, to: 1) Assess the relative contribution of genetic and environmental factors to variation in impulsivity at different life stages; 2) Determine the contribution of specific early experiences (maternal style, family social status, peer relationships) to variation in impulsivity; and, 3) Evaluate the role of serotonin and dopamine neurotransmitter activity in mediating genetic influences on impulsivity.

2. Indicate possible benefits to mankind and/or animals that may be derived from this study.

Impulsivity is a personality trait that contributes to vulnerability for a wide variety of behavioral, social and psychiatric problems, including substance abuse, hyperactivity, criminality and violence. This research will provide new information on specific genes that contribute to variation in this trait, and on interactions of genetic vulnerability with variation in family characteristics, social status and the quality of maternal care. It will lead to a better understanding of brain mechanisms that control impulsivity and impulsive aggression, and to improved pharmacological, social and behavioral interventions.

3. Explain the rationale for the use of animals, including (a) why the chosen species is the most appropriate for the study and (b) why the chosen species cannot be replaced with a phylogenetically lower species. Note that cost cannot be accepted as a justification.

The study subjects were born and currently reside in social groups at the VA Sepulveda Vervet Research Colony. This is a large multi-generational colony of animals that have been raised with their mothers, siblings and female kin in nturally composed social groups. As such, they provide an ideal population for behavioral genetics assessments. Paternity determination is now complete and genealogical relationships among colony members are known. Data on maternal behavior have already been collected for half of the subjects and family social status is known from birth. Results from this nonhuman primate colony will provide the first real opportunity to bridge the gap between rodent models and behavioral genetics studies of humans to increase our understanding of the relative role of specific genetic factors and early development within the normal range in the expression of impulsivity.

Experimental Design & Justification for Requested Number of Animals

1. Provide a two- to four-sentence lay description of the overall design written in language easily understandable to all members of the Committee, including those with non-scientific backgrounds. Verbatim text from grants is considered inappropriate for this section; those applications containing verbatim text from grants will not be accepted. The justification of the number of animals cannot be based on the frequency of the studies.

This is a longitudinal, developmental study that will follow vervet monkeys from birth to adulthood to determine the contributions of genetic, environmental and neurobiological factors to individual differences in impulsivity at different life stages. Genetic linkage analyses will be used to assess the contributions of candidate genes in serotonin and dopamine pathways to variation in this trait.

2. Provide a complete description of: (a) all activities involving the use of research animals; (b) a scientific justification for the total number of animals required to conduct this study. The number of animals justified in this section must match the totals in the Pain Category Assignments. To the extent possible, assign all animals to experimental groups, which can be easily distinguished by the independent variables defining each group (e.g.,drug dosages, time points, controls, etc.). Clearly indicate the number of animals needed per group and explain how group sizes were determined, either(i) by statistical methods, or (ii) where statistics are not applicable (e.g., teaching labs, feasibility studies, antibody production, etc.), on the basis of other considerations (e.g., student/animal ratio, tissue yield per animal, antigen/animal ratio, prior experience, etc.).

Tissue Collection

Please enter the following information regarding tissue collection for the protocol. See ARC Guidelines for Blood Collection in Laboratory Animals.

1. Tissue To Be Collected:

☑ Blood

☑ Other Collected: cerebrospinal fluid

2. Frequency of blood and/or other tissue collections:

Blood: 1-2 times per year
CSF: Once per year

3. Volume of blood and/or other tissue collected per time point:

Blood: 5-10 ml
CSF: 1 ml

4. Describe techniques that will be used to collect blood and/or other tissue.

Blood will be collected from the femoral vein using vacuutainer tubes. For CSF collection, the hair on the nape of the neck is shaved and the skin is scrubbed with betadine and isopropyl alcohol. Approximately 1ml of spinal fluid is drawn from the cisterna magna using a 22 guage 1.5 inch short bevel hypodermic needle.

5. Describe how anemia and infection will be prevented.

The volume of blood collected is not enough to cause anemia. The location of the blood draw is cleaned with alcohol, and the site of the CSF draw is scrubbed with betadine and isopropyl to prevent infection.

Non-Surgical Procedures

1. Describe all non-surgical procedures and experimental manipulations (e.g., imaging, behavioral studies, parkinsons and diabetes induction, chronic implant maintenance, cannulation)

Collection of behavioral data in the home groups for measures of maternal style, family social status and individual differences in sociability, anxiety and aggressiveness is performed without disturbing the animals.

Intruder Challenge Test
The Intruder Challenge Test is used to measure impulsivity and other dimensions of temperament in response to a social stimulus. It is performed in the home group. During a test session, all group members are locked into the indoor nightroom except for a subgroup of 3-4 individuals of the same age-sex class that are left in the outdoor area of the home enclosure. An unfamiliar adult animal in an individual cage is placed adjacent to the outer chain link fence and the subjects' responses are scored for 30 minutes. The impulsivity index derived from this test combines the latency to approach and the tendency to confront the stimulus animal aggressively. Impulsive animals rush into potentially dangerous situations and confront social strangers without taking time to evaluate the risks.

Novelty Challenge Test
For the novelty challenge, subjects are removed from the home group and transferred to an individual cage in the testing room at the VRC. They are presented with a series of three novel objects (a neutral stimulus, a puzzle feeder and a potentially threatening stimulus) within arms reach of the cage. Behavior is scored during stimulus presentation and control periods. At the end of the test session, subjects are anesthetized and a blood sample is collected to measure cortisol levels.

Activity

All animals currently living in the 16 naturally composed Core groups at the Vervet Research Colony will participate as subjects for this study. This includes 429 adults and 196 immatures that are part of a multigenerational extended pedigree. In addition, approximately 100 infants that are expected to be born in the next 2 years will be included in the sample, for a total of 725 animals studied at one or more points in development.

Measurement of developmental environment
Observational data on infant behavior and mother-infant relationships in the home are collected on 50 infants per year. These observations are performed without disturbing the animals.

Measurement of impulsivity
Animals will be tested in the Intruder Challenge test and the Novelty Challenge test at age 2, age 4, and twice as adults. Depending on the age of the animals when the 5-year study commenced, each individual will be tested between 1 and 3 times. The procedures for these challenge tests are described in NonSurgical Procedures section. These procedures involve only minimal disturbance to the animals and are listed as Category C.
The veterinarian, Dr. Schwiebert, asked if there was a mechanism in place to prevent biting injuries during the Intruder Challenge Test, and also asked if referred aggression ever occured among the test subjects. We have added the following to the description of this test in NonSurgical procedures section (#2): "If a fight did break out between a subject animal and the intruder, the four behavioral observers who are seated 10-15 feet from the intruder's cage during the test would intervene immediately and pull the intruder's cage out of reach. Redirected threats and displays among the subject males have never escalated to contact aggression during any of the tests."

Measurement of home group behavior
The behavior of all animals is recorded in the home group to measure individual differences in sociability, aggressiveness, and anxiety. Individual and matrilineal dominance rank is determined by behavioral observations of the direction of agonistic relationships in the home group. These observations are performed without disturbing the animals.

Neurobiological measures
Once per year, a sample of cerebrospinal fluid will be collected from each animal older than 20 months of age. The samples are collected during the annual health check and TB testing to minimize the number of times the animals are captured and anesthetized. A blood sample for genetic and hormone analysis will be taken at the same time. The CSF collection is listed as a Category D procedure. Of the 725 subjects, 675 will have one or more CSF samples. The 50 infants to be born in 2004 will not be sampled.

The resulting sample will include a total of 725 animals in a mixed cross-sectional longitudinal design. Modern genetic analysis of complex phenotypes requires large numbers of pedigreed animals in order to have sufficient power to detect effects of genes influencing such traits. Two levels of genetic analysis must always be evaluated when planning a study appropriate for genetic inference. Preliminary studies must have sufficient power to test whether or not a trait is heritable. More importantly, a study should be designed with adequate power to localize specific genes and genetic regions through linkage studies. The former type of study (classical quantitative genetics analysis) should be oriented around detecting genetic effects that account for as little as 10% of the total phenotypic variance. Linkage studies require substantially larger samples and should minimally be able to localize genes accounting for 20% of the total phenotypic variance. Given the breeding structure of the VRC with multiple generations and a large number of paternal half-sibships, empirical and simulation results suggest that having 500 animals available for genetic studies in extended pedigrees appears to meet both of these analytical requirements. With a sample of 500, we would have approximately 80% power to detect and localize genes accounting for 20% of the phenotypic variance in our measures of impulsivity.

The number of available subjects will vary for each of the longitudinal hypotheses being tested. For example, by the end of the study we will have data on behavioral and neurobiological phenotypes for 515 adult animals for classical heritability and genetic covariance analysis and for linkage to candidate genes in the serotonin and dopamine neurotransmitter systems.

Consistency of associations between temperament measures and indices of monoamine neurotransmitter activity from adolescence to adulthood will be assessed in 176 subjects, while the influence of maternal behavior on impulsivity in juveniles will be tested in 216 subjects. This represents the lower limit of sample size necessary to reliably detect the types of quantitative genetic effects we are proposing.

Animals participating in this study are already living in social groups at the colony. We anticipate that they will only be minimally disrupted by the procedures proposed here.

Pain Category Assignments

Please note that the Pain Category Letters have been changed to concur with those of the USDA.

NOTE: A painful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied. Examples of potentially painful/distressful procedures include, but are not limited to the following: terminal surgery; exuberant inflammation from adjuvants; ocular and skin irritancy testing; food or water deprivation beyond that necessary for normal presurgical preparation; noxious electrical shock that is not immediately escapable; paralysis or immobility in a conscious animal; extensive irradiation.

Category	Description
C	(Formerly Category A) Momentary or no pain/distress (Examples: injections of non-toxic substances; blood collections; euthanasia and harvesting of tissue only; observing natural behavior; behavioral testing without significant restraint or noxious stimuli.)
D	(Formerly Category B) Pain/distress relieved by use of appropriate anesthetics, analgesics, tranquilizers or by euthanasia (Examples: terminal surgery; survival surgery; ascites method of monoclonal antibody production; retroorbital blood collection, euthanasia of animals showing signs of more than slight or momentary pain and/or distress.)
E	(Formerly Category C) Pain/distress can not be relieved by use of anesthetics, analgesics, or tranquilizers, as the use of these agents would interfere with the experimental design (Examples: pain research; toxicity testing.)

Species:	Vervet Monkey
Strain (mouse):	
Average Weight:	infant
Sex:	Mixed
Pain Category:	C
Total Number of Animals Needed for the 3 Year Period:	50

Species:	Vervet Monkey
Strain (mouse):	
Average Weight:	juvenile to adult
Sex:	Mixed
Pain Category:	D
Total Number of Animals Needed for the 3 Year Period:	675

Pain Category

1. If the animals are listed under Pain Category D and/or E, check below all criteria that will be used to assess any potential pain/distress/discomfort in the animals. If applicable, include criteria used to evaluate post-operative pain/discomfort.

- ☑ Restlessness
- ☑ Vocalizing
- ☑ Loss of mobility
- ☐ Conjunctivitis, corneal edema, photophobia
- ☑ Licking, biting, or guarding a painful area
- ☑ Failure to groom, unkempt appearance
- ☐ Open sores/necrotic skin lesions
- ☑ Loss of appetite
- ☑ Weight loss.
  Percentage weight loss (max allowable 10%):
- ☑ Other: tremors or excessive drooling under ketamine anesthesia

2. If the animals are listed under Pain Category E, provide scientific justification indicating why pain/distress/discomfort-relieving methods will not be employed in this protocol.

NOTE: Procedures that may cause more than momentary or slight pain or distress to the animals must be performed with appropriate sedatives, analgesics or anesthetics, unless withholding such agents is justified for scientific reasons and will continue for only the necessary period of time.

The following questions must be answered for animals listed under Pain Category D and/or Pain Category E. Federal Regulations require that investigators consider alternatives (the 3 Rs - replacement, refinement and reduction) to procedures that may cause more than momentary or slight pain or distress to animals.

3. Consider all the alternatives listed below and explain why each of the following is not an available alternative for the proposed potentially painful/distressful procedure.

A. Replacement of animals with non-animal models (e.g., in vitro procedures, computer model) or a phylogenetically lower species:

The only category D procedure in this protocol is the collection of cerebrospinal fluid. This is a relatively noninvasive way to acquire information about the functioning of the brain. There are no in vitro procedures that could provide the necessary information about individual differences in neurotransmitter function to compare to behavioral and genetic differences between animals. A considerable amount of excellent research has been conducted with rodent models of behavior-genetic relationships. The research being conducted here goes beyond what is possible with rodent models by incorporating features of primate social organization, development and neurobiology that are more similar to humans.

B. Refinement of procedures in order to reduce the potential for pain/distress:

The procedure used to extract CSF takes only a few minutes. There have been no neurological complications of CSF collection in any of the >400 animals previously sampled by this research team. Only a small volume of fluid is extracted to reduce the likelihood of headaches following the procedure. The CSF sample is collected during the annual health examination and TB testing, thus reducing the distress and risk that would be caused by another roundup and ketamine administration.

C. Reduction in the number of animals proposed in this application (e.g., fewer animals involved in potentially painful procedures):

It is necessary to sample a large number of animals in order to conduct linkage studies of candidate genes with behavior and monoamine metabolite levels, as noted in the Experimental Design section.

Pain Literature Search

The following questions must be answered for animals listed under Pain Category D and/or Pain Category E.

Please note that according to PHS Policy IV.C.1.a, the Guide for the Care and Use of Laboratory Animals (the Guide p. 10) and USDA Animal Welfare Act Regulations §2.31(d)(1)(i) "procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals." Further, in order to meet the above-mentioned regulatory requirement and in accordance with UCLA's Animal Welfare Assurance on file with the National Institutes of Health Office of Laboratory Animal Welfare (OLAW), the Committee must ensure that the "principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources used to determine alternatives were not available." Please also note that the Committee recommends the use of keywords that are specific to the painful/distressful procedures you will be conducting and the animal model that will be used.

1. Indicate at least two databases or other sources consulted to support the conclusion that no alternatives are available.

- [x] Medline +
- [ ] PsychINFO
- [ ] Altweb
- [ ] UC Center for Alternatives
- [ ] Animal Welfare Information Center
- [x] BIOSIS
- [ ] Current Contents
- [ ] Other:

2. Combination of keywords used during the search (include each "and" & "or"):

serotonin and impulsivity
serotonin and gene# and impulsivity
serotonin and maternal and impulsivity and vervet
doapmine and impulsivity
dopamine and gene# and impulsivity
dopamine and maternal and impulsivity and vervet

PER 9/25/02 PI RESPONSE: The Pain Literature Search was also repeated on PubMed with vervet as a keyword. In this section, I kept the broader searches to aid in the identification of alternatives to the use of nonhuman primates in this type of research. The Pain Literature section of the RATS application was modified to reflect these changes. -jk

3. Date of Most Recent Search (MM/DD/YYYY):

09/20/02

4. Years Covered (e.g., 1980-2001):

1965-2002

Animal Care

This section must be posted with animals.

1. Will the experiments involve tumor formation?

The ARC requires daily monitoring of tumor growth and prohibits tumor growth beyond 1.5 cm in diameter in mice. Exceptions to this limit must be scientifically justified. Exceptions to this limit must be scientifically justified.

No

2. Will the experiments involve chronic disease (e.g., diabetes, chronic seizures, infections with disease agents)?

No

3. If the answer to either of the questions above is yes, describe the criteria for premature termination of the animals.

4. Will there be any special care instructions for animal husbandry?

No

5. Check below all that apply and convey special animal care requirements to the responsible veterinary staff.

- ☐ Temperature Range(s)
- ☐ Humidity
- ☐ Light Cycles
- ☐ Bedding/Litter changing schedules
- ☐ Water (e.g., sterile or deionized)
- ☐ Special diet/Feeding schedule
- ☐ Deprivation of food and/or water for reasons other than surgical preparation

6. Explain special care requirements in detail.

7. If you will be using transgenic animals in this research, please clarify whether there are any anticipated or suspected phenotypes of the transgenic mice that might cause pain or discomfort to the animals. If any pain, distress, or morbidity is associated with the phenotypes of this line, please indicate the criteria for premature termination of these mice.

Locations

Please indicate ALL locations including:

1. **where animals will be housed (vivarium housing and/or investigator-managed study area where animals will be housed for periods longer than 12 hours)**
2. **where research will be performed (research area where non-surgical procedures will be conducted)**
3. **where surgery will be performed, if applicable (surgery area)**

Please note that if vivarium housing has not been assigned, select "VIVARIUM" as the building name and "Unassigned" as the room number.

Building	Room	Species	Location Type
VA Sep	Hospital	Vervet Monkey	Research Area **Reason:** The research and housing will be at the VA Sepulveda Vervet Research Colony

Species Medications

List below all medications/agents that will be given to the animals to prevent or alleviate potential pain, distress, or discomfort associated with procedural or surgical protocols.

The selection of the most appropriate medication/agent should reflect that which best meets clinical and humane requirements without compromising the scientific aspects of the research protocol. In accordance with federal regulations, consultation with an attending veterinarian is required in the planning of a research protocol involving procedures that may cause more than momentary or slight pain or distress to the animals. Please note that according to the **ARC Guidelines on the Use of Pharmaceutical-Grade Compounds**, investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures.

ARC requires analgesics be provided to all animals recovering from major survival surgery for at least 48 hours after surgery, and then as needed. If post-operative analgesics will not be administered, animals must be listed in Pain Category E.

Drug Name:	ketamine
Species:	Vervet Monkey
Medication Type:	Anesthetic
Dose or Concentration:	8-10
Frequency:	1-2 times per year
Route:	im
Duration:	15 minutes
Purpose:	Other: CSF and blood collection

Species Euthanasia

For each species used, please provide the euthanasia information. Techniques for euthanasia must follow guidelines established in the current Report of the AVMA Panel on Euthanasia.

Species:

Vervet Monkey

What will be the final disposition of the animals?

Not Euthanized

Will anesthesia be used prior to use of the physical method of euthanasia?

No

For animals that will be euthanized by a physical method, please indicate that method.

If anesthesia cannot be administered, provide scientific justification.

Not applicable

For animals that will not be euthanized at the end of the study, please indicate the final disposition.

The vervets will continue to live in social groups at the VRC and will be available for other research protocols.
Individual animals that are suffering from progressive illnesses or injuries that are not responsive to veterinary care will be euthanized by chemical means. Euthanisia will be performed by the colony veterinarian.

Euthanasia Medication

This section is empty.

Following the novelty challenge blood sample collection, while the animal is still anesthetized, an activity meter (Minimitter Actiwatch) is attached to the animal's identification collar. The Actiwatch is a small watch-sized monitor (3cm x 3cm x 1cm) that records and stores data on movement. The animals wear the monitors in the home group for a two-week period. The data provide measures of average activity level, sleep cycles and circadian rhythms.

2. List probable clinical responses to and potential complications of the nonsurgical procedure(s).

Our past experience indicates that the animals show interest, excitement, and mild agitation when presented with the social and nonsocial stimuli. There is a potential for harm in the Intruder Challenge because the subjects can reach their hands into the intruder's cage, but in more than 150 trials with this test, no animal has been injured. If a fight did break out between a subject animal and the intruder, the four behavioral observers who are seated 10-15 feet from the intruder's cage during the test would intervene immediately and pull the intruder's cage out of reach. Redirected threats and displays among the subject males have never escalated to contact aggression during any of the tests.
There is also potential for harm during the roundup of the nonsubject animals and confinement to the nightroom. The Intruder Challenge tests are always performed when there are no small infants in the group to minimize the risk of injury. No animal has been injured in the nightroom or during the roundups for this test in more than 150 trials. The animals serving as the intruders are confined to an individual cage for up to 4 hours and care is taken to make sure that they have water and are protected from excessive heat or cold.

Animals first respond to the activity monitor by pulling at their collars, but all animals tested so far have adjusted within a day or two. The monitor is attached to the outside of the collar so it does not chafe against the animal's neck.

General Literature Search

Federal law requires the following information be provided regarding potential duplication of research efforts.

1. Indicate at least one database or other source consulted.

- [x] Medline +
- [ ] PsychINFO
- [ ] Altweb
- [ ] UC Center for Alternatives
- [ ] Animal Welfare Information Center
- [ ] BIOSIS
- [ ] Current Contents
- [ ] Other:

2. Provide the combination of keywords used during the search (include each "and" & "or"). You must provide at least two key words used in the search.

behavior and genetic# and impulsivity and vervet
maternal and impulsivity and vervet
development and impulsivity and vervet

PER 9/25/02 PI RESPONSE: I have modified the three-year renewal application to reflect the changes in the literature searches that the committee requested. For the General Literature Search to identify duplication of effort, PubMed was searched from 1965 to 2002 with vervet added as a keyword to narrow the focus of the search (search date 9/20/02). This new search is described in the RATS application. -jk

3. Date of Most Recent Search (MM/DD/YYYY):

09/20/02

4. Years Covered (e.g., 1980-2001):

1965-2002

Principal Investigator Assurance

This page must be completed by the Principal Investigator.

Regarding policies governing animal research at UCLA:

Yes	No	
◉	○	I agree to abide by all applicable federal, state, and local laws and regulations and UCLA policies and procedures.
◉	○	I agree to consult with an attending veterinarian prior to submission of the research protocol to the ARC.
◉	○	I declare that all experiments involving live animals will be performed under my supervision or that of another qualified scientist. All listed personnel will be trained and certified in the proper humane methods of animal care and use prior to conducting experimentation.
◉	○	I understand that emergency veterinary care will be administered to animals showing evidence of discomfort, ailment or illness.
◉	○	I declare that the information provided in this application is accurate to the best of my knowledge. If this project is funded by an extramural source, I certify that this application accurately reflects all currently planned procedures involving animals described in the proposal to the funding agency.
◉	○	Any modifications to the protocol will be submitted to and approved by the ARC prior to initiation of such changes.
◉	○	If this is a renewal application, I assure that appropriate progress has been made to justify the continued use of research animals.
◉	○	The experimental design has been refined in order to minimize the invasiveness of the proposed procedures.

Agreement on electronic submission:

I understand that by submitting this document that this document will be sent to appropriate members for review. I further understand that once submitted for review, this protocol cannot be modified or changed unless so requested by the ARC. In addition, once approved, all changes or modifications must be submitted for review and approval of the ARC prior to initiation.

Completed by: Lynn Fairbanks, 7/23/2002

FS Assurance

This section is empty.