**CNPRC**

**PROTOCOL FOR ANIMAL USE AND CARE**

*Email to: campusvet@ucdavis.edu*

**EH&S USE ONLY**

**CNPRC**

**PROTOCOL:** 10411  
**EXPIRES:** 12/19/03

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**Investigator**

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**Contact**

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**Species (common names):**

| Rhesus macaque | 18 | CRPRC |

**Number:**

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<tr>
<th>Source:</th>
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<tr>
<td>CRPRC</td>
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**Project Title**

Effect of vaginal CpG administration in rhesus macaques.

**Overnight housing location:**

CRPRC

**Day use:**

CRPRC (animal quarters or workrooms)

**Animals will be maintained by:**

[ X ] Vivarium  [ ] Investigator (If investigator maintained, attach husbandry SOP’s.)

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**Procedures:**

Provide a one or two sentence layman's description of the procedures employed on the animals in this project. This information will help the animal care staff understand any conditions they may encounter while caring for your animals.

Animals will be treated with CpG (cytosine and guanine linked by a phosphate)ODN (oligodeoxynucleotide) and monitored for one week.

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**Special Husbandry Requirements:**

Describe any special requirements your animals have with respect to food, water, temperature, humidity, light cycles, caging type, bedding, or any other conditions of husbandry.

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**Other instructions for animal care staff:** (check applicable entries)

**Sick Animals**

- [ X ] Call Investigator
- [ X ] Clinician to treat
- [ ] Terminate
- [ ] Necropsy

**Dead Animals**

- [ X ] Call Investigator
- [ ] Save for Investigator
- [ ] Bag for disposal
- [ X ] Necropsy

**Pest Control**

- [ ] Call Investigator
- [ X ] OK to use pesticides
- [ ] No Pesticides in animal area

**Hazardous Materials (only if in the animal room):**

- Infectious Agents?
  - [ ] Yes  [ X ] No
  - Agent(s):

- Radioisotopes?
  - [ ] Yes  [ X ] No
  - Agent(s):

- Chemical Carcinogens?
  - [ ] Yes  [ X ] No
  - Agent(s):

- Toxic Chemicals?
  - [ ] Yes  [ X ] No
  - Agent(s):
Funding source: NIH, NIAID

Previously approved? [ ] Yes [X] No

Is the project already funded? [X] Yes [ ] No

Previous protocol number (if any): 

**Summary of Procedures:**

**a)** Briefly describe the **overall intent** of the study. Include in your description a statement of your hypothesis, the objectives and significance of the study. Your target audience is a faculty member from a discipline unrelated to yours. Do not use jargon.

The hypothesis of this study is that administration of CpG’s (a mimic of bacterial DNA) will generate innate immune responses upon intravaginal administration. Thus far, CpG’s have not been tested intravaginally in the rhesus macaque model. The information we have regarding the protective effects of CpG’s in the monkey model are from respiratory studies in cynomolgus macaques. Therefore, we propose this pilot study using three concentrations of CpG’s in order to determine what dose is appropriate in the rhesus intravaginal model prior to pathogenic challenge studies.

**b)** Procedures employed in this project:

Please check the appropriate boxes if any of these procedures will be employed in your project:

- [ ] Monoclonal Antibody Production **
- [ ] Polyclonal Antibody Production **
- [ ] LD 50 or ID50 studies.
- [X] Catheters, blood collection, intubation
- [ ] Prolonged restraint. (8 hrs+)
- [X] Fasting prior to a procedure.
- [ ] Food or water restriction
- [ ] Non-recovery surgical procedures
- [ ] Survival surgical procedures
- [ ] Multiple survival surgery
- [ ] Behavioral modification.
- [ ] Induced illness, intoxication, or disease
- [ ] Death as an endpoint (see i below)
- [ ] Trapping, banding or marking wild animals
- [ ] Aversive conditioning.

**If this protocol only describes antibody production, you may use the attached antibody production page in lieu of completing section c below.**
c) Describe the use of animals in your project in detail, with special reference to any of procedures checked above. Include any physical, chemical or biological agents that may be administered. List each study group, and describe all the specific procedures that will be performed on each animal in each study group. Use terminology that will be understood by individuals outside your field of expertise. (Note: This cell will expand to whatever length you require. You may make this section as long as you wish, but try to be concise. Some projects may require one or two pages.)

One of the ways the immune system is able to detect microbes is through recognition of unmethylated CpG dinucleotides (CpG motifs) by toll-like receptors. These motifs are common in bacterial DNA, but are under-represented and methylated in vertebrate DNA. Thus, this difference in the DNA allows the immune system to detect foreign microbes and elicit an immune response. Synthetic CpG’s have been made in order to take advantage of this ability to activate the immune system. Three CpG’s with slight variations in structure (A, B, C) will be used in these experiments. They have been tested for immunogenicity and toxicity in rodents. The results show generation of an immune response with no adverse effects reported. Study timeline below:

For all groups: We request mature, cycling female rhesus macaques. For all procedures, animals will be fasted 12 hours prior to immobilization using ketamine (6-10 mg/kg for bleeds and lavages, 20 mg/kg for intravaginal CpG administration according to CNPRC standard operating procedures) which will be administered intra-muscularly. Buprenorphine (0.01-0.03 mg/kg) will be administered for post-procedure pain according to the CNPRC veterinary staff.

Group A- Intravaginal administration of 1 mg CpG ODN-A will generate local and systemic immune responses.

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On Day 0, 1 mg of CpG-ODN-A dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

Group B- Intravaginal administration of 1 mg CpG ODN-B will generate local and systemic immune responses.

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On Day 0, 1 mg of CpG-ODN-B dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected...
on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group C - Intravaginal administration of 1 mg CpG ODN-C will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 1 mg of CpG-ODN-C dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group D - Intravaginal administration of 5 mg CpG ODN-A will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 5 mg of CpG-ODN-A dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group E - Intravaginal administration of 5 mg CpG ODN-B will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 5 mg of CpG-ODN-B dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group F - Intravaginal administration of 5 mg CpG ODN-C will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 5 mg of CpG-ODN-C dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group G - Intravaginal administration of 10 mg CpG ODN-A will generate local and systemic immune responses.**
Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 10 mg of CpG-ODN-A dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group H- Intravaginal administration of 10 mg CpG ODN-B will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 10 mg of CpG-ODN-B dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

**Group I- Intravaginal administration of 10 mg CpG ODN-C will generate local and systemic immune responses.**

Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected 14 days and 7 days prior to the CpG ODN administration. On day 0, 10 mg of CpG-ODN-C dissolved in 1 ml sterile phosphate buffered saline will be administered intravaginally (by atraumatically inserting a 1 ml syringe). This process will be repeated 24 hours later. Blood (10-20 mls, not to exceed 12 ml/kg/month) and vaginal lavages (by atraumatically inserting a pipette into the vagina and washing with PBS) will be collected on Day 0, 12 hours, 24 hours, 48 hours, 96 hours and 7 days after the first CpG administration. Animals will be rested for a period of at least two months before assignment to a CpG/SIV challenge study. (approved protocol 10216, once we have the results from this study an amendment will be filed)

d) Study Groups and Numbers: Define, in the form of a table, the numbers of animals to be used in each experimental group described above. The table may be presented on a separate page as an attachment to this protocol if you prefer. The Normal format should be three columns: Study Group, Procedure, Number of animals. The number of rows should follow from the number of study groups; you may add as many rows as you require. The chart must fully account for the number of animals you intend to use under this protocol. Assign each group to an invasiveness category according to the chart below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Procedures / Drugs</th>
<th>Number of Animals</th>
<th>Category</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Intravaginal 1 mg CpG-A and SIV</td>
<td>2</td>
<td>2</td>
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<tr>
<td>B</td>
<td>Intravaginal 1 mg CpG-B and SIV</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>Intravaginal 1 mg CpG-C and SIV</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>Intravaginal 5 mg control and SIV</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>E</td>
<td>Intravaginal 5 mg CpG-A and SIV</td>
<td>2</td>
<td>2</td>
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<tr>
<td>F</td>
<td>Intravaginal 5 mg CpG-B and SIV</td>
<td>2</td>
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<tr>
<td>G</td>
<td>Intravaginal 10 mg CpG-C and SIV</td>
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<tr>
<td>H</td>
<td>Intravaginal 10 mg control and SIV</td>
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<td>2</td>
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<tr>
<td>I</td>
<td>Intravaginal 10 mg CpG-A and SIV</td>
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### Categories of invasiveness

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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| 1        | Little or no discomfort or stress  
**Examples:** domestic flocks or herds being maintained in simulated or actual commercial production management systems; the short-term and skillful restraint of animals for purposes of observation or physical examination; blood sampling; injection of material in amounts that will not cause adverse reactions by the following routes: intravenous, subcutaneous, intramuscular, intraperitoneal, or oral. |
| 2        | Minor stress or pain of short duration  
**Examples:** cannulation or catheterization of blood vessels or body cavities under anesthesia; minor surgical procedures under anesthesia, such as biopsies or laparoscopy; short periods of restraint beyond that required for simple observation or examination, but consistent with minimal distress |
| 3        | Moderate to severe distress  
**Examples:** major surgical procedures conducted under general anesthesia, with subsequent recovery; prolonged (several hours or more) periods of physical restraint; induction of behavioral stresses such as maternal deprivation |
| 4        | Severe pain near, at or above the pain tolerance threshold  
**Examples:** exposure to noxious stimuli or agents whose effects are unknown; exposure to drugs, chemicals, or infectious agents at levels that markedly impair physiological systems and which cause death, severe pain, or extreme distress; surgical experiments which have a high degree of invasiveness. |

Further descriptions of these categories are included in the instructions following this document.

e) Rationale for species and numbers: How did you determine that 1) the species choice was appropriate and 2) the number of animals in each study groups was the minimum number necessary to achieve sound scientific results?

The rhesus macaque animal model is the most generally accepted model predication of human immune responses and primates must be used for pre-clinical studies involving intravaginal administration of CpG-ODN and its effects on local and systemic immune responses. Two animals are sufficient to determine whether or not a detectable immune response is generated by the CpG ODN treatment. We have based the dosages used in this study on results from a respiratory study in cynomolgous macaques. This pilot study will be used to determine if the proposed dosages are sufficient to elicit a protective immune response prior to starting pathogenic challenge studies.

f) Surgery: If the project involves survival surgery, where will the surgery be conducted?

Who will be the surgeon?

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| g) Anesthetics, Analgesics, Tranquilizers, Neuromuscular blocking agents: |

Post procedural analgesics should be given whenever there is possibility of pain or discomfort that is more than slight or momentary. If postoperative analgesics are not to be given, justify the practice under part (f) below.

Provide the following information about any of these drugs that you intend to use in this project.

<table>
<thead>
<tr>
<th>Species</th>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>When and how often will it be given?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhesus</td>
<td>Telazol</td>
<td>6-20mg/kg</td>
<td>IM</td>
<td>Before all procedures</td>
</tr>
<tr>
<td>rhesus</td>
<td>buprenorphine</td>
<td>0.01-0.03mg/kg</td>
<td>IM</td>
<td>As needed in judgement of CRPRC vets</td>
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h) Neuromuscular blocking agents can conceal inadequate anesthesia and therefore require special justification. If you are using a neuromuscular blocking agent, please complete the following:
Why do you need to use a neuromuscular blocking agent?

What physiologic parameters are monitored during the procedure to assess adequacy of anesthesia?

Under what circumstances will incremental doses of anesthetics-analgesics be administered?

i) Adverse effects:
Describe any potential adverse effects of the experiment on the animals (such as pain, discomfort; reduced growth, fever, anemia, neurological deficits; behavioral abnormalities or other clinical symptoms of acute or chronic distress or nutritional deficiency)

Any injection or venipuncture has the potential to cause minor pain or discomfort, but the animals are immobilized for the procedure and should not experience pain.

CpG-ODN administration at extreme dosages could possibly result in septic shock. Doses up to 100 ug have been used in the rodent system, and 1 mg/kg in the respiratory cynomolgous macaque model with no adverse effects reported. A 10 mg dose (the highest dose proposed in this study) in the rhesus macaque is within the same mg/kg dose range, and therefore should not induce adverse effects. As a precaution, animals should not be treated with TNF (Tumor necrosis factor)-alpha during these studies due to the slim possibility of inducing TNF-alpha mediated shock.

How will the signs listed above be ameliorated or alleviated? If signs are not to be alleviated or ameliorated by means of post-operative analgesics or other means, explain why this is necessary.

All possible efforts will be made to minimize animal pain and discomfort. Analgesics have no effect on the proposed studies and they will be administered at the discretion of the CRPRC veterinary staff. If for some reason an animal goes into shock, it will be treated according to the CRPRC veterinary staff and will not be treated with further CpG-ODN.

Note: if any unanticipated adverse effects not described above do occur during the course of the study, a complete description of those effects and the steps taken to mitigate them must be submitted to the committee as an amendment to this protocol.

Is death an endpoint in your experimental procedure? [ ] Yes [X] No
(Note: “Death as an endpoint” refers to acute toxicity testing, assessment of virulence of pathogens, neutralization tests for toxins, and other studies in which animals are not euthanized, but die as a direct result of the experimental manipulation). If death is an endpoint, explain why it is not possible to euthanize the animals at an earlier point in the study. If you can euthanize the animals at an earlier point, describe the clinical signs which will dictate that an animal will be euthanized.

j) Literature search for alternatives and unnecessary duplication:

Federal law specifically requires this section. You are required to conduct a literature search to determine that either 1) there are no alternative methodologies by which to conduct this class/lab, or 2) there are alternative methodologies, but these are not appropriate for your particular class/lab. “Alternative methodologies” refers to reduction, replacement, and refinement (the three R’s) of animal use, not just animal replacement. You must also show that this use of animals is not unnecessarily duplicative of other studies.

UC Davis provides on-line access to a number of databases that can be used to search for alternatives. Visit http://trc.ucdavis.edu/jawelsh/Databases_Med_Vet_Researchers.htm (email: jawelsh@ucdavis.edu)
What was the date on which you conducted this search?  

11/26/02

List the databases searched or other sources consulted (there should be more than one). Include the years covered by the search.

<table>
<thead>
<tr>
<th>Database Name</th>
<th>Years Covered</th>
<th>Keywords / Search Strategy</th>
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<tbody>
<tr>
<td>Reference Update</td>
<td>1999-present</td>
<td>CpG motifs, CpG, pathogens, immune response, virus, primates</td>
</tr>
<tr>
<td>Current Contents</td>
<td>1990-present</td>
<td>CpG motifs, CpG, pathogens, immune response, virus, primates</td>
</tr>
</tbody>
</table>

What were your findings with respect to alternative methodologies?

CpG oligodinucleotides have been shown to induce immune responses in tissue culture systems, rodent models, and a small number of cynomolgous monkeys. So far, we are not aware of intravaginal use in the rhesus macaque system. The rhesus macaque animal model is the most generally accepted model predication of human immune responses and primates must be used for pre-clinical studies involving intravaginal administration of CpG-ODN and its effects on local and systemic immune responses.

CpG ODN are being tested in various forms to treat allergies and cancer, as well as viral pathogens. They are particularly attractive because they can provide resistance against a broad spectrum of pathogens. Other adjuvants/agents have been tried with variable success.

Has this study been previously conducted?  [ ] Yes  [X] No

If the study has been conducted previously, explain why it is scientifically necessary to replicate the experiment.

k) Disposition of animals: At what point in the study, if any, will the animals be euthanized?

Animals will not be euthanized, they will be rested for at least two months and assigned to a CpG/SIV challenge study.

l) Methods of euthanasia: Even if your study does not involve killing the animals, you should show a method that you would use in the event of unanticipated injury or illness. If anesthetic overdose is the method, show the agent, dose, and route.

<table>
<thead>
<tr>
<th>Species</th>
<th>Method</th>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>route</th>
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<tbody>
<tr>
<td>rhesus</td>
<td>IV</td>
<td>pentobarbital</td>
<td>60 mg/kg</td>
<td>IV</td>
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m) Surplus animals: What will you do with any animals not euthanized at the conclusion of the project?

They will be assigned to a CpG treatment followed by SIV challenge study.
**Project Roster:** Please provide the names of all the individuals who will work with animals on this project. This page will not be made available to the public. Give either the University Employee ID # or a valid UC Davis email address so that we can document training and occupational health compliance for regulatory agencies. Include all investigators, student employees, post-doctoral researchers, staff research associates, post-graduate researchers and laboratory assistants who will actually work with the animals. You don’t need to include the staff of the vivarium in which your animals will be housed.

The principal investigator is responsible for keeping this roster current. If any staff is added or subtracted from this project, you must amend the protocol by sending the campus veterinarian a memo describing any changes.

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<th>Last Name</th>
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**Occupational Health Program:**

Supervisors must enroll their employees in the campus Occupational Health Program if the workers are at increased risk of illness or injury (such as allergy, physical injury, or infectious disease) because of their work. Enroll workers by having them complete an "Animal Contact History Form", available from Employee Health Services (phone 752-2330). For further information, visit our web site at [http://ehs.ucdavis.edu/animal/health/](http://ehs.ucdavis.edu/animal/health/) or read the UC Davis Policy & Procedure Manual 290-25.

**Training:**

Supervisors are responsible for insuring that their employees are adequate trained, both in the specifics of their job and in the requirements of the Federal Animal Welfare Act. EH&S offers free, basic wet labs in laboratory animal handling and techniques, and lecture format classes in the requirements of the Animal Welfare Act. To schedule a class for your unit, contact EH&S at 2-2364. Information is available on the world wide web at [http://ehs.ucdavis.edu/](http://ehs.ucdavis.edu/).
Assurances for the Humane Care and Use of Vertebrate Animals:

Principal Investigator's Statement:

I have read and agree to abide by the UC Davis Policy and Procedure Manual section 290-30 (Animal Use and Care). This project will be conducted in accordance with the ILAR Guide for the Care and Use of Laboratory Animals, and the UC Davis Animal Welfare Assurance on file with the US Public Health Service. (These documents are available from the Campus Veterinarian and at http://ehs.ucdavis.edu/). I will abide by all Federal, state and local laws and regulations dealing with the use of animals in research.

I will advise the Animal Use and Care Administrative Advisory Committee in writing of any significant changes in the procedures or personnel involved in this project.

__________________________________________
Principal Investigator

__________________________
Rank / Title

__________________________
Date

Committee Use Only Below

** Conditions necessary for Committee Approval:


Final Disposition of this protocol:

[ ] Approved

[ ] Not Approved

[ ] Withdrawn by Investigator

Date of Action: _____/_____/_____

I verify that the Institutional Animal Care and Use Committee of the University of California, Davis, acted on this protocol as shown above.

____________________________________
Campus Veterinarian

__________________________
Date