INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)
CALIFORNIA STATE UNIVERSITY, BAKERSFIELD
9001 Stockdale Highway, Bakersfield, CA 93311-1099

MINUTES OF MEETING
Friday, 30 January 2004
Old Pub/Runner Café

Members Present:
Scientific Concerns: David Germano, Todd McBride, Steve Suter
Non-Scientific Concerns: Andrew Troup, Jane Granskog
Community Issues: Debby Kroeger, Martin Murdock
Veterinarian: Mylon Filkins

Members Absent:
No Safety/Risk Management Officer has been appointed

Visitors:
Dee Bailey and Isabel Sumaya, Psychology, for Protocols 04-01 and 04-02
Carol Raupp, Psychology

Meeting was called to order by Chair Steve Suter at 12:56 PM.

PREVIOUS MINUTES:

Granskog moved and Kroeger seconded, a motion to approve the minutes for the IACUC meeting of 03 October 2003. The motion was approved unanimously.

ANNOUNCEMENTS: [none]

OLD BUSINESS:

Online Training. Most of the IACUC members have done the online training in Humane Care and Use of Animal Subjects. There was general satisfaction with decisions about who should take which modules. Notes of errors/corrections will be forwarded to the IACUC Chair for action.

NEW BUSINESS:

Protocol Reviews

a. **Protocol 04-01 [**Isabel Sumaya, Psychology**]** "Circadian Effects of Melatonin on Extrapyramidal Side Effects in Rats Treated with Typical and Atypical Antipsychotics"

Following introductions, the investigators summarized the proposed research. This is continuation of a 3-4 year series of projects. Melatonin is a neurohormone and is circadian sensitive, increasing in the dark phase. A handout was provided on previous research results with rats showing that fluphenazine causes hypokinesis when administered in dark phase, but not in the light phase. When melatonin is

combined with fluphenazine, hypokinesis is greatly diminished. They want to look at other anti-psychotics, including the more recently developed atypical anti-psychotics which have less extra-pyramidal effects. The bar apparatus was demonstrated, on which the rat's forepaws will be placed as a test of hypokinesis. The investigator indicated that she has used this test hundreds of times. Questions followed:

Q: You are studying acute effects. Drugs are administered chronically. Wouldn't that perhaps be different? **A:** Yes, dopaminergic effects emerge with extended use. We would want to look at that eventually. This model is analogous to schizophrenia only in a limited way.

Q: Adminstration of anti-psychotics with humans is normally oral, isn't it, whereas you will be injecting the drugs? **A:** Yes, and there are compliance problems with oral administration. It is possible that this research could help with that. We will be using intraperitoneal administration.

Q: How will the drugs be stored? **A:** They will be stored in a locked cabinet inside a locked lab room.

Q: Does this study require the CSUB Drug Enforcement Administration license? **A:** No, these are not scheduled drugs. **Q:** It would be a good idea to treat these drugs as if they were scheduled drugs to establish a tracking system.

Q: Does hypokinesis mean that the animal is conscious and paralyzed? **A:** No, the animal is not paralyzed. The effect of the drug is limited to voluntary movement.

Q: But a person would be quite distressed to experience this, wouldn't they? **A:** Yes, as in Parkinson's disease. This is something we are hoping to ameliorate though research such as this.

Q: Has a relationship been shown between the anti-psychotic effects of the drugs and their hypokinetic effects? **A:** No, there are not yet adequate animal models of schizophrenia. One of the purposes of this line of work is to see if melatonin and dopamine are in the same neurochemical system.

Q: Do you think that there would be different effects of anti-psychotic drugs in humans administered in light vs. dark phases? **A:** Yes, I just proposed a human study for that in the morning IRB/HSR meeting.

Q: Are you looking toward human clinical trials eventually? **A:** Yes, would be fairly easy since melatonin isn't a scheduled drug.

Q: Are there any behavior signs of distress that you can use to determine the distress of the animal? Comment from IACUC member: Can't tell, it's not moving [jokingly] [Visitor made a loud exclamation and stormed from the room.]

Q: How many research assistants will you be training? **A:** Two.

Q: Why will these students be participating? **A:** They want to work with animals. Most of them have taken biological psychology and research methods.

Q: Are there also educational benefits going on? **A:** Yes, there is a lot of education going on in the research setting.

[Visitor returned, the IACUC member who made the above comment apologized, and was thanked by the visitor.]

Q: The number of animals used is 144. **A:** Yes, but they will be used in smaller batches. A total of 60 will move on to the Protocol 04-02 research. All animals will get re-used, including in the Psyc 301, Principles of Learning Lab course.

Q: Will be housing 144 at one time? **A:** Yes, all will be housed at once. There is room for that and funding has been provided for that.

Q: Are there any social problems housing such animals together? **A:** Only with mice, but not with rats. In fact, there is plenty of evidence that this is beneficial for rats.

Q: Is there sufficient space to accommodate both Todd's and Isabel's animals? **A:** Yes.

The investigators and the visitor were asked to leave the room and discussion followed among the IACUC members. A motion was offered to unconditionally approve the protocol. [Murdock moved, Filkins seconded, unanimously approved] The investigators and visitor returned and the IACUC Chair explained the decision.

b. Protocol 04-02 [Isabel Sumaya, Psychology**]** "The Effects of Caloric Restriction in an Animal Model of Depression in Rats"

Reduced caloric intake is associated with longer life spans in laboratory rats and lowered incidence of some chronic diseases. However, the serotonergic neurotransmitter system is also depressed, which has been implicated in depression in humans. Here, they wish to explore the possible relationship between caloric restriction and depression using an animal model, with the amount of immobility during a forced swim test as an index of helplessness, which is often associated with depression in humans and is taken as a depression analog in non-human animals. They are also interested in possible circadian effects. Questions followed:

Q: What if they don't swim. An IACUC member has found that some don't. **A:** I have never had one sink in hundreds of uses of this test. Perhaps there are species differences.

Q: The apparatus is set up so they are confined and cannot climb out? **A:** Yes, it's a large cylinder filled with water.

Q: Would changes in catecholamines effect swim test performance? **A:** Yes, that would be expected.

Q: Would time to immobility be as good a measure as seconds of immobility over the 6-minutes duration of the test? That way the rats would experience less stress. **A:** No, that would not work, because rats alternate between swimming and just floating.

Q: What is the extent of caloric restriction? **A:** They will be taken down to 80% of their free-feeding body weight and maintained there.

Q: It seems like the control issue that you need to be concerned with is muscle *endurance*, not muscle *strength*. Those are very different variables and there are well-established different standard measures of these. **A:** [It was not clear in their response that the investigators make this distinction in their thinking. McBride offered to provide methodological guidance on this.]

Q: So, if you are hungry you may live longer, but you will be depressed, is that the expectation at this point? **A:** Yes.

Q: You will have them swim until they give up. So, the point is to make them suffer. **A:** The point is to stress them to the point that they give up.

Q: Are there other ways of measuring depression or learned helplessness in rats? **A:** Yes, but these paradigms seem to involve more pain and suffering. For example, there are procedures based on electric shock and use of hot plates. All anti-depressants are tested by the FDA using the forced swim test, so we also have the advantage of a very large research literature with this test.

Q: What is the rationale for using a duration of 6 minutes? There would be less stress with a shorter duration. **A:** Earlier research has arrived at the 6-minute standard, so this is really the minimum that could be used. A shorter duration, 4 minutes is often used for mice, and some investigators use a much longer duration, as much as 15 minutes, for rats.

Q: Are there adverse effects of the swim test? **A:** There are no adverse effects that can be seen from the rats' behavior.

Q: What if they are just weaker because of the caloric restriction? **A:** It's probably the opposite, plus we are using the wire-hanging test to control for that.

Q: Is this a rat study leading to eventual research with humans? **A:** Yes, depending on the results of this and related studies.

Q: Note that there is a typo on p. 9 in the sentence dealing with unnecessary duplication.

The investigators and the visitor were asked to step out and the IACUC members engaged in further discussion. Conditions of approval were established. These were:

1. The typo about unnecessary duplication on p. 9 must be corrected.

2. The Orleans [1990]/Shapiro & Field [1987] rated "anticipated pain and distress" should be changed to Level #4, "Protocols that cause moderate pain or stress to vertebrate species."

A motion was offered to conditionally approve the protocol. [Filkins moved, Granskog seconded, unanimously approved] The investigators and visitor returned and the IACUC Chair explained the decision.

AREAS OF CONCERN:

After the visitors had left, IACUC members discussed the IACUC custom of allowing visitors to participate freely in meetings in terms of speaking and particularly in terms of questioning investigators. It was agreed that visitors should not be allowed to address/question investigators presenting protocols [as has been the custom of the IACUC thus far]. The dilemma of even having visitors present while the IACUC discusses protocols that are not yet public information was noted, but openness of the meeting was valued. The following procedure was adopted on a trial basis:

> "The present IACUC custom is to allow visitors to attend IACUC meetings and to address comments to and ask questions of investigators presenting protocols to the IACUC. This structure was reviewed at the IACUC meeting of 30 January 2004. It was agreed that it is desirable for visitors to attend meetings and to provide input on protocols under consideration, even though protocols only become public information after they have been approved. However, it was agreed that visitors *should not* be allowed to direct comments to investigators or question investigators. It was decided that, on a trial basis, the following format would be used for consideration of protocols:
>
> 1. The investigator presents a brief, oral overview of the written protocol that has been submitted for review.
> 2. IACUC members ask questions of the investigator, who then leaves the meeting.
> 3. Any visitors who wish to address the IACUC do so and then leave the meeting.
> 4. The IACUC considers the protocol in executive session.
> 5. Investigators and visitors return to the meeting and the decision of the IACUC is announced."

NEXT MEETING:

Friday, 23 April 2004 - "Old Pub" 12:30 p.m. – Lunch 1:00 p.m. - Meeting

ADJOURNMENT:

There being no further business, the meeting was adjourned at 3:00 PM. (Grankog moved, Murdock seconded, approved unanimously).

Online training and testing with the Human Care and Use of Animal Subjects modules was considered the Winter 2004 training for IACUC members.

Respectfully Submitted,
Steve Suter, Professor of Psychology, Secretary for the IACUC