May 4, 2006

Edward H. Hammond
Director
The Sunshine Project
PO Box 41987
Austin, TX 78704

Dear Mr. Hammond,

Please find enclosed the minutes from Origen Therapeutics' Institutional Biosafety Committee meetings from July 2003, April 2004 and February 2005. These minutes are from all of the IBC meetings that have occurred since 1 May 2003, as you have requested.

In answer to your question regarding our policies on experiments in the seven areas of concern identified by the report *Biotechnology Research in an Age of Terrorism* (the Fink Committee report), the Origen Therapeutics IBC reviews all experiments involving potentially infectious agents or recombinant DNA molecules and thus we have procedures to identify, review and oversee all experiments that might be of concern. No research in any of those categories of concern has been performed at Origen Therapeutics.

Sincerely,

Philip Leighton, Ph.D
Chair, Institutional Biosafety Committee
Origen Therapeutics
1450 Rollins Road
Burllingame, CA 94010

Origen Therapeutics Institutional Biosafety Committee Meeting
February 16, 2005
Minutes

1. Welcome all members of the Origen Therapeutics Institutional Biosafety Committee

The composition of the Origen Therapeutics Institutional Biosafety Committee for 2004 is listed below with three new members.

Chair	Lei Zhu, Ph.D., Origen Therapeutics (Replaced Dr. Babette Heyer on May 3, 2004)
Origen Therapeutics	Robert Etches, Ph.D. Phil Leighton, Ph.D.
Community Representatives	Kristina Bonham, Ph.D., Vistagen (Replaced Dr. Ondine Callan on May 3, 2004) Kari Roberts, MBA (Replaced Dr. Claudia Fieger on June 17, 2004)

2. Review the minutes from the last IBC meeting (April 6, 2004).

The following topics were discussed at the last IBC meeting:

The most important issue from the last meeting was the use of lentivirus at Origen Therapeutics. The lentivirus used at Origen is a vector for introducing DNA into cells in culture or into live chickens. The lentivirus is replication-defective and won't replicate or spread on its own. We use the lentivirus kit from Invitrogen; BSL2 laboratory practices are recommended by the manufacturer. At the last meeting we went over the guidelines from the CDC handbook for BSL2 practices. Rooms were designated specifically for virus work: for cell culture, we use a cell culture room which is equipped with a biosafety cabinet. A separate set of pipets is set aside for virus use and filter tips are employed. For embryology, a biosafety cabinet is used for injecting the embryos with virus, which is done with a mechanical micro-pipet. Also recommended were: a separate incubator in a separate room for embryo incubation after injection; a training session for personnel using lentivirus; no fabric-type chairs in the lab or carpeting. All of these recommendations have been implemented.

At the last meeting, two new protocols were approved: IBC-009 from Babette Heyer, and IBC-010 from Phil Leighton.

We have heard from the Sunshine Project and have responded to their request for meeting minutes.

The next IBC report is due March 5 2005.

3. Update on research projects

No new protocols were submitted during the last year.
One new protocol had been under review at the time of the last committee meeting; Lei Zhu signed it after it completed review.
Addenda to two previously approved protocols were reviewed and approved by the Origen Therapeutics IBC during 2004. The committee members reviewing addenda are usually the same as those who reviewed the original application since they are already familiar with the protocol.

Principal investigator	Protocol number	Project title
Babette Heyer, Ph.D.	IBC009 Addendum	Minor modification of existing protocol "Generation and evaluation of a lentiviral vector for the production of transgenic chickens" (Reviewed and approved on 7/6/04 by the IBC chair without full committee review)
	IBC009 Addendum 2	Modification of existing protocol (Reviewed and approved on 8/16/04 by two committee members without full committee review)
	IBC009 Addendum 3	Modification of existing protocol (Reviewed and approved on 10/13/04 by two committee members without full committee review)
	IBC010 Addendum 4	Modification of existing protocol (Reviewed and approved on 1/14/05 by two committee members without full committee review)
Phil Leighton, Ph.D.	IBC010	Human Polyclonal Antibody

	Production in Chickens (Reviewed at 4/6/04 IBC meeting and revised version approved by full committee on 5/11/04)
IBC010 Addendum	Minor modification of existing protocol (Reviewed and approved on 8/13/04 by the IBC chair and one committee member without full committee review)
IBC010 Addendum 2	Minor modification of existing protocol (Reviewed and approved on 11/23/04 by the IBC chair and one committee member without full committee review)

4. Review lentiviral related research program under Biosafety Level 2 condition at Origen Therapeutics

The committee chair reviewed the following procedures that are in use at Origen Therapeutics:
Direct handling of virus is to be done under BSL2 conditions.
Standard procedures have been established according to the CDC handbook.
Viral-infected cell culture is done in a biosafety cabinet in a dedicated room.
Embryology work is done in a biosafety cabinet.
Embryo injection is done by mechanical injection device, not mouth pipet.
Lentivirus-injected embryos are incubated in dedicated incubators in a separate room.
New users are trained in the use of lentivirus. Records of who was trained are signed off by people present and by the IBC chair.

In the last year, the training manual was revised to include more detail and distributed to those who are trained in lentiviral procedures.
The issue of lentivirus being grown in the same lab room as cultured cells was referred to the IACUC since it is more an animal welfare issue than a biosafety issue.

5. Other business

Everyone agreed that we had covered everything necessary.

Origen Therapeutics Institutional Biosafety Committee Meeting
April 6, 2004
Minutes

1. Welcome all members of the Origen Therapeutics Institutional Biosafety Committee

The composition of the Origen Therapeutics Institutional Biosafety Committee for 2003 is listed below.

Chair	Babette Heyer, Ph.D., Origen Therapeutics
Origen Therapeutics	Robert Etches, Ph.D. Phil Leighton, Ph.D.
Community Representatives	Ondine Callan, Ph.D., Vistagen
	Claudia Fieger, Ph.D

2. Review of the Agenda for today's meeting

1) Review the minutes from the last meeting (July 15, 2003) and from the walk through
2) Summary of IBC work over the past few months
3) Discuss biosafety issues related to the proposed use of lentivirus at Origen.
4) New protocols from Babette Heyer and Phil Leighton

3. Review of the last IBC meeting (July 15, 2003)

At the last IBC meeting, the pigeons living in the attic of the building were discussed. It was decided that this is not an IBC issue but should be referred to Bob for pest eradication. Rodent control is also now in effect.
The cell culture waste is now disposed of properly (liquid waste is collected and sent out; plasticware is autoclaved).
Everything the committee had recommended previously is now in practice.

4. Review of the last few months.

At the beginning of the year we got a request from the Sunshine Project, an activist group following biodefense related activities. This was triggered by Phil Leighton's grant on biodefense. They asked for the minutes from the last 2 IBC meetings, which it is within their right to do. Babette Heyer sent the minutes from the two sets of approved minutes – minutes from the last meeting hadn't been approved yet. She sent them and hasn't heard anything back yet.

Lei Zhu's protocol appendum was approved without review, IBC-003B. Since it was a short addendum, Babette Heyer approved it without full committee review.

Babette Heyer sent out the annual report to the NIH and got a letter back from them saying it was approved. We must file the next report by March 5, 2005.

5. The proposed use of replication-incompetent lentivirus at Origen.

Babette Heyer stated she is planning to order a kit for lentivirus production from Invitrogen. Invitrogen recommends BSL2 conditions.

We went over the guidelines for BSL2 from the CDC handbook. Babette told us that for growing the virus in cell culture, the "DT40 room" is equipped with a hood that is already classified as class II type A biosafety cabinet, which will be sufficient for BSL2. This is the most suitable room for growing the virus. It was agreed that pipets will be set aside for virus use to reduce the possibility of cross contamination with DT40/ALV virus, and procedures will be adopted to minimize the possibility.

The Embryology lab has a similar biosafety cabinet that is sufficient (the shell cutting hood). Rob suggested we may need to get a new front on the hood in embryology in order to fit a microscope in the hood.

After virus injection, embryos will be incubated in Octagon incubators. Ideally, one octagon will be taken out into another room. Christine had recommended putting it into the old kitchen in the front, so that it is separate from the rest of the eggs. Everything coming out will be autoclaved.

The issue of potential ALV infection (coming from the DT40 room) of the chicks was discussed. It was decided that it would be best to test for ALV at the time of lentivirus injection. In addition, the IACUC and our vet Pat Wakenell will be consulted.

It was suggested and agreed that we have a training session for those who will work with BSL-2 level agents.

6. New protocols.

IBC-009 "Generation and evaluation of a Lentiviral vector for the production of transgenic chickens" PI: Babette Heyer

Babette Heyer left the room for the discussion.
The following requests were made for the application to be approved:

- Should have labels on the plasmid maps, state less then 1/3 the viral genome, make it clear on the map itself what is what.

- State which parts of the plasmids make it BSL-2 vs. BSL-1. Color code or some way make it clear.
- Statement of how the virus is made
- Line 0 chickens are not ideal and not necessary because lentivirus is different sequence from chicken endogenous viruses. Don't need to restrict to line 0, but keep it in as a possibility.

IBC-010 " Human polyclonal antibody production in chickens" PI: Phil Leighton. He left the room for the discussion.

The following requests were made for the application to be approved:

- Should add the different construct variants for the 2 constructs he applied for (as shown yesterday in the Scientist meeting) and get them all approved at the same time.
- The protocol should be signed by the PI and the personnel involved when submitted.

7. IBC committee member changes.

Babette Heyer announced she is stepping down as chair at end of month. Claudia Fieger also informed us that she might step down soon, too, since she is looking for a new position. She will inform the committee if and when she steps down. Ondine suggested that Kristi Bonham from Vistagen replace her as an external IBC committee member.

July 15, 2003
Origen Therapeutics Biosafety meeting Minutes
9 am.

The meeting started at 09:00 with the following present: Ondine Callan, Babette Heyer, Claudia Fieger, Rob Etches, and Phil Leighton.

Babette Heyer went over the minutes from the last meeting (January 21, 2002), indicating the following issues were discussed:
- For work on human and primate cells, it was decided a tissue culture room should be designated, a sign posted at door, waste should be de-contaminated with bleach, and lids should be used on waste bins for plastic ware.
- An insect and rodent control program should be in effect.
- Employees working with human cells should be offered immunizations to Hepatitis B.
- The move to the new building at 1450 Rollins road, and the biosafety issues relevant to having the company spread over two buildings.
- Approval of biosafety protocols
- Peggy's e-mail appended to the end of the minutes. It was agreed that her points were valid and should be included in the biosafety manual. Babette agreed that she would add a paragraph at the beginning of the biosafety manual and then distribute the new version to employees.

Babette then gave the committee an update on what has been done since the last meeting:
- Since we haven't worked with human or primate cells, we haven't put up a sign yet, and we haven't started decontamination procedures or used lidded trash cans.
- The insect and rodent control program is active, according to Rob.
- Babette had talked to Bob about immunizations, which are currently available. She had also reminded the employees of this fact.
- The move to the new building is currently on hold.

Babette suggested we use lids on the wastebaskets in cell culture.
(Rob said he would look into getting wastebaskets with lids, but it turned out we already have some).

Claudia asked about cell culture liquid waste, such as cell culture supernatants – at UCSF, for example, everything is bleached. Currently we pour it down the drain. She suggested we bleach it too. All agreed we should bleach the liquid waste before dumping down the drain.

Babette brought up general cleanliness issues at Origen and the fact that we don't have a janitor. As an example we discussed the fungus growth along the edge of the floor in autoclave room last winter. An e-mail to Bob was ignored. Babette bleached the fungus and Christine cleaned the area. It was thought that for now it's ok that things are not too clean since we keep the animal room very clean and keep good control over animal waste, which is the most important.

Rooms with transgenic cells or embryos should be locked, as we talked about last time. However, the incubator room door needs to be open during warm periods or the incubators will become too hot, so we can't keep it locked all the time. Rob raised the question of whether it was really a serious problem to not have them locked.
Claudia suggested posting a warning sign to keep unauthorized people out of the incubator room in order to cover our legal responsibility for when the doors are open. It was agreed that Babette will post signage.

Babette told the committee that she sent a report to the NIH about our IBC, including the meeting minutes from the last meeting, a copy of our biosafey manual, and c.v.'s of the committee members. The response was positive. The NIH asked that we send an annual report once per year, in March. They seemed pleased to get the report.

Review of new protocols:

Lei Zhu. Lei's previous protocol was IBC 003. Since her new protocols are essentially the same experiments, her protocol number will be IBC 003-B for the new constructs. Both new constructs and old constructs are described in her protocol. The most relevant part for biosafety is the CX promoter. Rob said that Lei is thinking of changing some of the restriction sites for linearization – but Babette and Phil said the constructs will be essentially the same and that we don't need a new version of the protocol.
Claudia would like to see added a simple sentence about what the constructs are going to be used for, and what the goal of the experiment will be. Babette pointed out that this information is stated briefly in section B. Claudia was not fully satisfied with that and would still like another sentence added.
Phil would like Lei to clarify maps so that the monoclonal cassette is clearly labeled on Figures 3 and 5.
All agreed that if Lei provides these changes, the protocol is approved.

Marie-Cecile van de Lavoir. IBC007 and 008.
Claudia indicated that the descriptive statements were helpful.
Rob was wondering about MC1-tk; are we going to use it? Is it expressed? We answered that it would only be used if we had hundreds of clones and wanted to try to reduce the numbers by negative selection against TK.
No other comments.
All agreed we should approve IBC007.
All agreed we should also approve IBC008.

IBC 003-B:
Babette will send it around again when changes have been made.

Babette brought up the cell culture waste lids and bleach and signs. Bob will be consulted. Babette suggested someone in cell culture should make the changes there. We also need a sign in Embryology. Rob suggested that the committee insist that we use lids in cell culture.
Babette will send e-mail to everyone about what we have decided.