Guide to Submission

California Stem Cell, Inc.
Submission #2012-ACD-001

Note: Two undated documents, "Procedure for Presenting Informed Consent to Study Subjects" and a protocol were submitted, but California Stem Cell stated that they could not confirm that the documents were in use at the time of embryo donation, so they are not included here.

2

hESC Registry Application Database

Detailed Listing for Request #: 2012-ACD-001
May 14, 2012

hESC Registry Application Search Results

Request #: 2012-ACD-001
Status: Pending

Review: ACD

Assurance: Yes (Section II(B))
Certification: Yes
Authority: Yes

Cell Lines: 1
Available: 0

Previous #:
2012-DRAFT-008

Email
Edit
Delete
Switch to ADM

Organization: California Stem Cell, Inc.
Org Address: 18301 Von Karman. Ave., Suite 130 Irvine, CA 92612
DUNS: 787412233 **Grant Number(s):**
Signing Official (SO): Kenneth Berger / 949-201-9633 / ken@californiastemcell.com
Submitter of Request: / /
Submitter Comments: (None)

Line #1: CSC14
NIH Approval #:
Available: Other - Other - Unknown at this time, but potentially available in the future.
Embryo from U.S.: Yes
Embryo Donated in Year(s): 2006
Provider Name: California Stem Cell, Inc.
Provider Phone: 949-201-9633
Provider Email: ken@californiastemcell.com
Provider URL: www.californiastemcell.com
Provider Restrictions:

NIH Restrictions:

Additional Information:

Supporting Documents:
Document 1: (PDF - 04/11/2012) Cover Letter
Document 2: (PDF - 04/03/2012) Procedure for presenting informed consent to study subjects.
Document 3: (PDF - 04/03/2012) De-identified signed consent form for embryo used to derive CSC14 line.
Document 5: (PDF - 04/03/2012) De-identified consent form signed at fertility center to donate frozen embryos to research.
Document 6: (PDF - 04/03/2012) IRB approval of protocol used to procure frozen embryos. Obtained retrospectively.
Document 7: (PDF - 04/11/2012) Study protocol for procurement of excess embryos from IVF for use in hESC research.

Administrative Comments: Document 4 deleted per submitter request 16 April 2012 E. Gadbois

11 May 2012 Submitter Response Email - DHannemann 14 May 2012

Cryopreservation Program Participation Agreement (11 May 2012 email attachment - 1 of 2) - DHannemann 14 May 2012

CSCI Request to WCFC for Cryo Form (11 May 2012 email attachment - 2 of 2) - DHannemann 14 May 2012

Administrative Attachments:
Document 1: (PDF - 04/20/2012) Compilation PDF
Document 2: (PDF - 04/23/2012) NIH questions to CSCI 13 April 2012
Document 3: (PDF - 04/16/2012) 16 April 2012 response from CSCI
Document 4: (PDF - 04/23/2012) Questions to CSCI 23 April 2012
Document 5: (PDF - 05/14/2012) 11 May 2012 Submitter Response Email
Document 6: (PDF - 05/14/2012) Cryopreservation Program Participation Agreement (11 May 2012 email attachment - 1 of 2)
Document 7: (PDF - 05/14/2012) CSCI Request to WCFC for Cryo Form (11 May 2012 email attachment - 2 of 2)

Status History:
Draft: 03/28/2012
Pending: 04/11/2012

Emails Sent: 04/11/2012-New_Applicaton_Email

Previous ADM Request Number:
Switched from ADM to ACD Date: 04/10/2012
Reason for Switch to ACD Review:
Per submitter request

Added By: Commons\KENNETHBERGER **On:** 03/28/2012 | **Last Updated By:** NIH\hannemannd **On:** 05/14/2012 | **Record ID:** 104

Total Record Count = 1

Administration Page

Logout of NIH Form 2890 Admin Site

California Stem Cell

April 11, 2012

National Institutes of Health (NIH)
NIH Stem Cell Registry

Dear Advisory Committee to the Director (ACD),

Re: Cell Line CSC14 Request

California Stem Cell, Inc. (CSC) has been advised to submit our registry cell line request directly to the ACD. We had previously submitted our request to the NIH Administrative Review (ADM). However, the 2006 consent form (document 3) for the donation of CSC14 contains all the elements of Section IIA, except for Element 8 (withdrawal procedure). The study protocol (document 7) that was retrospectively approved by a third party IRB (document 6) does contain all the elements of Section IIA, including Element 8. But because CSC does not have any direct evidence that the donors were notified of their right to withdraw as described in Element 8, we are submitting our request to you, the Working Group of the ACD.

All supporting information for this request is in English. Also, the documents provided to, discussed with, and signed by the donors were in English.

The supporting information includes the following documents:

1. Cover Letter
2. Procedure for presenting informed consent to study subjects.
   (Elements: 1,2,4,7 and part of 8)
3. De-identified signed consent form for embryo used to derive CSC14 line.
   (Elements: 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15)
4. Informed consent template used in this study. Identical to document signed by donors.
   (Elements: 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15)
5. De-identified consent form signed at fertility center to donate frozen embryos to research.
   (Elements: 1, 2, 3, 7)
6. IRB approval of protocol used to procure frozen embryos. Obtained retrospectively.
   (Element: 16)
7. Study protocol for procurement of excess embryos from IVF for use in hESC research.
   (Elements: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15)

Thank you very much for your consideration in registering our cell line.

Sincerely,

Kenneth L. Berger, PhD
Director, Regulatory Affairs
California Stem Cell, Inc.
18301 Von Karman Ave., Suite 130
Irvine, CA 92612
P: 949-201-9633
F: 949-725-1756

WEST COAST FERTILITY CENTERS
Advanced Reproductive Technology and Microsurgery

[redacted] *Medical Director*
Diplomate, American Board of Obstetrics and Gynecology
Reproductive Endocrinology and Infertility

JUL 3 1 2006

Date: [redacted]

Dear [redacted]

Fees for: [redacted]

RE: DISPOSITION OF FROZEN EMBRYOS / OOCYTES.

The contract pertaining to the storage of your frozen material in our Laboratory has expired. You must select one of the options below and return this form within two weeks.

1. Continue storage of frozen embryos/oocytes for an **oneyear fee of $500**.

PATIENT SIGNATURE **SPOUSE/PARTNER SIGNATURE**

2. Discard the embryos/oocytes according to the Center's policy.

PATIENT SIGNATURE **SPOUSE/PARTNER SIGNATURE**

3. Donate your frozen embryos/oocytes to another infertile couple.

PATIENT SIGNATURE **SPOUSE/PARTNER SIGNATURE**

4. Donate your frozen embryos/oocytes to West Coast Fertility Centers for research. You will receive a more detailed research consent.

[redacted]

If you wish to continue storage, please enclose payment for $500. If after 30 days from this notice West Coast Fertility Centers has not received any contact from you, we will consider your participation in the Cryopreservation Program terminated and the embryos will be considered abandoned under the terms of our Cryopreservation Program Participation Agreement. If you have any questions, please contact [redacted] in our Laboratory: (714) 513-1399 x 120.

Please return this letter with your decision to:

West Coast Fertility Centers
11160 Warner Ave Suite 411
Fountain Valley, CA 92708

[redacted], M.D., Medical Director
West Coast Fertility Centers

AUG 16 2006

WEST COAST FERTILITY CENTER
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Consent for Embryo Donation

CSC 14

Name of Donor(s): [redacted]

The purpose of this agreement is to obtain your written consent for the donation of excess or frozen embryo(s) that were produced for you as part of your infertility treatment with [redacted] M.D., Inc. dba West Coast Fertility Center ("WCFC") which was conducted in accordance with the terms and conditions of that Cryopreservation Program Participation Agreement dated 8/11/06 between you and WCFC.

Your agreement to donate your embryo(s) is completely voluntary. Your choice to donate or not to donate your embryo(s) will have no affect on the treatment you receive from WCFC. Because the election to donate your embryo(s) is strictly voluntary, before you sign this agreement and agree to donate your embryo(s), it is important that you read and discuss this agreement with someone at WCFC so that you understand and are comfortable with what will happen to your embryo(s) after they are donated. If, after reading this agreement and discussing the use of your embryo(s) with representatives of WCFC, you decide that you do want to make the donation, you will need to sign this agreement which will confirm your consent to allow your embryo(s) to be used for the purposes described below. Of course, before you sign this agreement and agree to donate your embryo(s) to research, you must first decide that they are no longer needed for your infertility treatment and that you would like them to be used in research.

PURPOSE/PROCEDURES

Your embryo(s) will be used under National Institutes of Health and National Academy of Sciences guidelines to develop human embryonic stem cells and human pluripotent stem cell lines. Stem cells are cells with the unique capacity to divide an unlimited number of times. A stem "cell line" means a group of cells that can live and divide outside of the body. A "pluripotent" stem cell line is a stem cell line that is capable of developing into a wide variety of cell types. The cells that will be used to derive the stem cell lines will be cells from either your cleavage stage embryo(s) or the inner cell mass of your embryo(s). The cells that will be used cannot develop into embryos nor can they be implanted into a woman's uterus.

The stem cells and stem cell lines that we hope to create from your embryo(s) will be used in research about human development, in transplantation research, in testing new pharmaceuticals and, if possible in the future, for therapeutic uses on humans.

The stem cells and stem cell lines derived from your embryo(s) may be frozen and kept for many years. It is contemplated that your embryo(s), and the stem cells and stem cell lines derived therefrom, will be used by the University of California, Irvine ("UCI") in research

[redacted] Initial

being conducted by Dr. Hans S. Keirstead. However, depending on UCI's needs, some of your embryos, or the stem cells or stem cell lines derived from your embryos, may also be shared with, made available to, or transferred to other qualified researchers both in the for-profit and not-for-profit sectors. Your embryos, or the stem cells or stem cell lines derived from your embryos, may also be used by a for-profit entity other than WCFC in which Dr. [redacted] or Dr. Keirstead may have an ownership interest called California Stem Cell, Inc. ("CSCI") which is engaged in stem cell research.

COMMERCIAL DEVELOPMENT

Under federal law, if you do not sign this agreement, you would have the right to control the use of the stem cell lines derived from your embryo(s). However, by signing this agreement, you are giving up that right and authorizing the use of your embryo(s) for the research described in the PURPOSE/PROCEDURES section of this agreement. By signing this agreement, you also authorize WCFC, UCI, CSCI and others to use your embryo(s) and any stem cells or stem cell lines derived from your embryo(s) in any lawful way, including future research studies, transferring them to other for-profit or not-for-profit entities, or even destroying them should they no longer be required.

Samples obtained from your embryo(s) in this research may lead to discoveries that could be patented or licensed to for-profit or not-for-profit entities. You will receive no financial compensation should this occur. However, should WCFC, UCI or CSCI ever provide your embryo(s), stem cells or stem cell lines derived from your embryo(s) to a third party for any purpose, your privacy will be scrupulously protected and your identity will not be revealed. All of the protections described in the CONFIDENTIALITY section of this agreement will be followed. In addition to your anonymity being maintained, under no circumstances will you have any responsibility or liability for any use that may be made of your donated embryo(s).

RISKS

If you agree to donate your embryo(s), those embryo(s) will no longer be available for use in your infertility treatment program.

BENEFITS

Although there will be no direct medical benefit to you, it is the hope of the research scientists who will be using your embryo(s) that other people will benefit in the future through the research that is conducted on the stem cell lines derived from your embryo(s). The purpose of the research at UCI and CSCI is to advance scientific and medical knowledge.

[redacted]
Initial

COSTS AND COMPENSATION

You will not be compensated for the use of your embryo(s), nor will it cost you anything to donate your embryo(s). The decision to donate your embryo(s) will have no effect on the cost of your past or future IVF treatment with WCFC.

ALTERNATIVES TO DONATING YOUR EMBRYO(S)

If you choose not to donate your embryo(s), they will continue to be stored or otherwise handled according to the terms and conditions of the Cryopreservation Program Participation Agreement between you and WCFC.

FUTURE ACCESS TO INFORMATION

Once you donate your embryo(s), you will not be given information about what becomes of them or what is learned from working with the embryo(s) you donate or the cells or cell lines that are created from your embryo(s). Because of the anonymity of your donation, which is more particularly described in the CONFIDENTIALITY section, your donation is and must be made without restriction or direction as to the types of research which may be conducted or who may receive the cells or cell lines which may be derived from your embryo(s). However, as stated above, none of your embryos will be implanted into another woman's uterus or used to create a life.

CONFIDENTIALITY

If your embryo(s) are not already be in the possession of WCFC, the embryo(s) you donate will first be transferred to WCFC, which, in turn, will transfer them to UCI or CSCI. Before the embryo(s) are transferred from WCFC, the embryologist at WCFC will assign a randomly generated identification number to the embryo(s). Only this number will be transferred to UCI, CSCI or any other third party, and no patient specific or identifying data will be provided to any other person who might come into possession of or work with your embryo(s) or the cells or stem cell lines derived from your embryo(s). In other words, all of the information which identifies the embryo(s) as having been created by you (e.g., your name, address or other identifying information) will be protected by WCFC, and the only information that will ever leave WCFC about the identity of the embryo(s) will be the randomly generated identification number. Even if the research results in the publication of scientific papers or results in a therapy or patentable product, no information that identifies you or could link the embryo(s), stem cells or cell lines to you will be disseminated or made available.

[redacted]

Initial

SIGNATURE AND CONSENT

By signing this agreement, you are giving your permission for WCFC, UCI, CSCI and others to use and store the embryo(s) you donate in the manner and for the purposes set forth in the PURPOSE/PROCEDURES section of this agreement. In addition, by signing this agreement, you are specifically authorizing your embryo(s) to be used to create stem cells or stem cell lines and for those stem cells and stem cell line to be kept for as long as they remain useful and to used by and shared with other qualified researchers both in the for-profit and not-for-profit sector in research about human development, in transplantation research, in testing new pharmaceuticals and, perhaps one day for therapeutic uses on humans. By signing this agreement, you further understand that the stem cells or stem cell lines derived from your embryos may be used by CSCI, a for-profit entity in which Dr. [redacted] or Dr. Keirstead may have an ownership interest

DONOR

[redacted]

BioMed·IRB

IRB Meeting Date: November 11, 2009 **Expiration Date:** November 11, 2010

BIOMED IRB INITIAL APPROVAL NOTIFICATION

Study Title: PROCEDURE FOR PROCUREMENT OF EXCESS EMBRYOS FOLLOWING IN-VITRO FERTILIZATION TREATMENT TO BE USED FOR THE DERIVATION OF NEW EMBRYONIC STEM CELL LINES

Sponsor: California Stem Cell, Inc.

Protocol Number: CSC-0902

Protocol Date: November 5, 2009

Principal Investigator: Chris N. Airriess, PhD

Approved Facilities: West Coast Fertility Centers
11160 Warner Ave., Suite 411
Fountain Valley, CA 92708

BioMed IRB has approved the above referenced study as having satisfied the criteria for research on November 11, 2009. Chris N. Airriess, PhD, as Principal Investigator was approved for the above referenced study at the November 11, 2009 meeting. The designated facilities were approved for this study at the November 11, 2009 meeting. The IRB has granted approval for research to be conducted only to those sites that are listed under the entitled "**Approved Facilities**" section of this letter.

The IRB committee has determined that the risk assessment for this study is Minimal.

It was the determination of the IRB Committee that, in this instance, an Informed Consent document is not necessary.

The IRB has determined that continual review of this study will occur Annually.

Approximately thirty days before November 11, 2010, you will be required to complete a Continuing Review Report Form. Continuing review is the responsibility of the Principal Investigator. If you do not receive this form, please contact the IRB office immediately. The Continuing Review Report Form must be received by the due date to allow ample time for ongoing review before the study's expiration date.

(12)

IRB approval is granted conditional on your adherence to the following requirements:

- The information submitted to the IRB is true and correct.
- Research will be conducted in accordance with the approved protocol.
- All materials used to recruit study subjects must be pre-approved by the IRB.
- Additional safeguards will be followed when vulnerable subjects, such as children or minors, are participants in the study.

The investigator agrees to report the following information to the IRB:

- Serious Adverse Events occurring at your site should be reported within ten (10) calendar days from the date of discovery by the investigator.
- Serious Adverse Events (IND Safety Reports) occurring at other sites should be reported no later than thirty (30) days from the date of discovery.
- Any changes in the research activity (i.e. changes in study staff, facility etc.) should be reported promptly. In addition, the investigator will not make any changes in the research without the IRB's approval, except when necessary to eliminate apparent immediate hazards to study subjects.
- Any other unanticipated problems involving risks to study subjects.
- Any other unanticipated problems involving risks to the intergrity of the data for this study.

BioMed IRB is comprised of a diverse group of individuals in accordance with the Federal Regulations and the International Conference on Harmonization guidance for Good Clinical Practice. BioMed IRB follows written procedures for performing review, documenting meeting minutes, disclosure of member conflict of interest prior to deliberation or voting, as well as the retention of all records containing research materials as required by the Code of Federal Regulations (21CFR parts 50 and 56; and 45 CFR part 46).

On behalf of the BioMed IRB, I certify that the information contained in this letter is true and correct as verified by the minutes and records of the BioMed IRB.

Please keep a copy of the application material, as well as a copy of this letter, in your files for future reference. Should you have questions or concerns, please do not hesitate to contact this office.

Sincerely,

Authorized Signature	Study Manager Title
Cecilia Barrena Printed Name	November 11, 2009 Date

CC: Rania Nasis, MD, MBA, California Stem Cell, Inc.

From: Ken Berger
To: HESCREGISTRY (NIH/OD)
Cc: Kattarina Phu
Subject: Re: Quick question--can respond by noon Pacific time today?
Date: Tuesday, May 22, 2012 1:39:04 PM

Hi Ellen,

As I stated in my previous email, "In 2006 CSC was unaware that an IRB approval was necessary for embryo donation." Therefore I doubt that CSC had a Federal Wide Assurance in 2006. I went on the FWA website and searched for CSC and there were no documents. I am aware that an institution must have an FWA in order to receive HHS support for research involving human subjects. We were not receiving HHS support in 2006, nor are we now.

Should CSC register our current IRB and obtain an FWA now? I certainly will do that if you think it will be a good idea.

I hope this answers your question. Thanks again for your help.

Best,

Ken

--

Kenneth L. Berger, Ph.D.
Director of Regulatory Affairs
California Stem Cell, Inc.
18301 Von Karman Ave, Suite 130
Irvine, CA 92612
P: 949-201-9633
F: 949-725-1756

On Tue, May 22, 2012 at 7:49 AM, HESCREGISTRY (NIH/OD) <hescregistry@mail.nih.gov> wrote:

> Hi Dr. Berger,
>
> The Working Group has another question. If you are able to respond by noon Pacific time today, that would be very helpful. Can you check whether California Stem Cell had a Federal Wide Assurance in 2006 (at the time the embryo was donated and the time the line was derived)?
>
> Please feel free to call me at 301-594-2567 if this question isn't clear.

Sincerely,

Ellen Gadbois

From: Ken Berger [mailto:ken@californiastemcell.com]
Sent: Friday, May 11, 2012 12:39 PM
To: HESCREGISTRY (NIH/OD)
Subject: Response to Working Group Questions

Hi Ellen,

I am responding to the questions from the Working Group:

1) Could you please provide a copy of the "Cryopreservation Program Participation Agreement" that is referenced on page 1 of the embryo donation consent? Please send a redacted copy of the form signed by the embryo donors or a blank form that is the version signed by the embryo donors.

A blank copy of the "Cryopreservation Program Participation Agreement" is attached to this email (Attachment 1). Also see an email from CSC to the fertility clinic requesting the actual version of the form used in 2006 (Attachment 2).

2) Please explain when the protocol was developed and if it was in effect at the time of the embryo donation.

I have no direct evidence to support that the protocol (or an earlier version) was in effect at the time of the embryo donation.

3) Was IRB approval for this protocol sought at the time that the embryo was donated? If not, please explain why not.

As mentioned in the cover letter to our application, the BioMed IRB approval was obtained retrospectively. The date of embryo consent was August 2006 and IRB approval was November 2009. In 2006 CSC was unaware that an IRB approval was necessary for embryo donation.

4) Please explain when, for whom, and for what purposes the "Procedure for Presenting Informed

Consent to Study Subjects" was written. Was this document provided to the embryo donors?

I have no direct evidence that the form "Procedure for Presenting Informed Consent to Study Subjects" (or an earlier version) was in effect at the fertility clinic in 2006.

5) Please describe the role of the individual whose name was redacted on the top of page 2 of the embryo donation consent as a person who “may have an ownership interest called California Stem Cell Inc.”

The attending physician at the West Coast Fertility Clinic (WCFC) had his name redacted on the consent form for personal reasons.

To summarize:

1. CSC has presented evidence that the donors of CSC14 received and signed:

    a. The blank “Cryopreservation Program Participation Agreement”

    b. The redacted Consent Form “Disposition of Frozen Embryos/Oocytes” (July 31, 2006)

    c. The redacted “West Coast Fertility Center Consent to Act as a Human Research Subject” (August 16, 2006)

2. CSC has no direct evidence that the following documents or earlier versions thereof were in effect in 2006:

    a. “Procedure for Presenting Informed Consent to Study Subjects”

    b. “Procedure for the Procurement of Excess Embryos Following In-Vitro Fertilization Treatment to be Used for the Derivation of New Embryonic Stem Cell Lines”

3. As stated in the Cover Letter of our application, CSC believes that the consent form that was signed by the donors contains all the elements of Section II (A) of the NIH Guidelines except for Element 8.

I hope that my answers are sufficient. Thanks again for your help.

Best,

Ken

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Kenneth L. Berger, Ph.D.
Director of Regulatory Affairs
California Stem Cell, Inc.

18301 Von Karman Ave, Suite 130
Irvine, CA 92612
P: 949-201-9633
F: 949-725-1756

CRYOPRESERVATION PROGRAM PARTICIPATION AGREEMENT

This Cryopreservation Program Participation Agreement and Informed Consent ("Agreement") is made on _____ among David G. Diaz M.D., Inc. dba West Coast Fertility Centers ("WCFC"), and _____ ("Patient") and _____ ("Partner").

RECITALS

A. Patient and Partner are attempting to achieve a pregnancy by means of WCFC's Assisted Reproductive Program.

B. To assist some of its patients in achieving a pregnancy, WCFC offers a Cryopreservation Program ("Cryo Program") to qualified patients. Cryopreservation (freezing) is a clinical procedure at WCFC that is designed to initiate a successful pregnancy after thawing cryopreserved human embryos or eggs. Participation in this clinical procedure is voluntary and if Patient and Partner elect not to participate, their decision will not affect their relations with WCFC in any manner, except that Patient and Partner will no longer have those embryos or eggs available for our use in either WCFC'S or anyone else's infertility treatment program.

C. With knowledge that their participation is voluntary, Patient and Partner desire to enroll in WCFC's Cyro Program on the terms and conditions set forth below.

AGREEMENT

1. <u>Patient's and Partner's Representations</u>. Patient and Partner represent to WCFC that they have consulted with, or have had the opportunity to consult with, such advisors as were necessary to enable them to decide to participate in the Cryo Program.

2. Sperm and Egg Contributions. Partner agrees to provide his sperm, and Patient agrees to provide her oocytes (eggs) to WCFC to be used in the Cryo Program. (If donated sperm or eggs are to be used, a separate form must be signed concurrently with this Agreement.)

3. Cryopreserved Material. WCFC will use its best efforts to achieve fertilization of one or more of Patient's eggs. If more eggs are retrieved and/or fertilized than are presently desirable for transfer into Patient, the embryos or unfertilized eggs (as applicable) which are not being currently transferred will be cryopreserved (frozen) by WCFC in order to preserve them for later transfer into Patient. (In cryopreserved form these embryos and eggs will be referred to as "Cryopreserved Material"). Patient and Partner acknowledge that the Cryopreserved Material has no capacity to produce human life until an egg or embryo has been thawed and properly transferred into the Patient. Patient and Partner also acknowledge that the process of thawing an egg, producing an embryo and transferring the embryo into the Patient is not achievable in all instances, and that the process may not work for Patient and Partner, despite the best efforts of WCFC.

4. Use of the Cryopreserved Material. WCFC will maintain, utilize or dispose of the Cryopreserved Material in the following manner:

a. So long as both Patient and Partner remain in the Cryo Program, the Cryopreserved Material will be stored exclusively for the benefit of Patient and Partner and used, after consultation with Patient and Partner, to assist Patient in achieving a pregnancy.

b. Upon termination of Patient's and Partner's participation in the Cryo Program (as defined in Section 5, below), unless otherwise provided for in this Agreement, all of Patient's and Partner's interest in the Cryopreserved Material will pass to WCFC, at which time

WCFC will destroy the Cryopreserved Material following standard medical laboratory procedures for elimination of bio-hazardous material. If this Agreement terminates for any of the reasons set forth in paragraphs 5(c)iii, 5(c)iv or 5(c)vii, WCFC will give Patient and Partner 90 days prior written notice (as provided in Section 12) before destroying the Cryopreserved Material.

c. In the event a dispute arises between Patient and Partner, or between Patient, Partner and WCFC, with respect to the Cryopreserved Material, WCFC will maintain the Cryopreserved Material in its frozen state at Patient's and Partner's expense, until a final court order is entered telling WCFC what to do with the Cryopreserved Material.

5. <u>Payment/Term/Termination</u>.

a. During the term of this Agreement (defined below), Patient and Partner shall pay to WCFC the following professional fees for the cryopreservation (freezing) of their embryos or eggs:

i. $700 for the preparation of the Cryopreserved Material and storage of the Cryopreserved Material for two years after the initial freezing; and

ii. $600 for the one year extended term storage fee if Patient and Partner extend the term of this Agreement under paragraph 5(b), below.

b. The term of this Agreement shall be two years from the date that Patient's Cryopreserved Material first becomes available for use in the Cryo Program. At the end of the two year term, Patient and Partner must either transport their Cryopreserved Material to a long-

term storage facility other than WCFC or execute a written agreement extending the term of this Agreement for one additional year. Ninety days prior to the termination of this Agreement, WCFC will give Patient and Partner notice of the termination date of the Agreement and their options under this Agreement.

c. This Agreement may be terminated by either Patient and Partner or WCFC upon the happening of any of the following events:

i. Patient and Partner advise WCFC in writing that they want to end their participation in the Cryo Program and terminate this Agreement. Patient's and Partner's signatures must be notarized.

ii. A final court order: (1) orders the termination of Patients and Partners participation in the Cryo Program; (2) directs WCFC to deliver to Patient, Partner or some third party all, but not less than all, of the Cryopreserved Material; or (3) directs WCFC to destroy all, but not less than all, of the Cryopreserved Material

iii. This Agreement reaches the end of its two year term and it is not extended in writing.

iv. In the opinion of WCF's medical director, Patient's physical condition changes such as to render her incapable of receiving a transfer or of carrying a pregnancy to term.

v. If either Patient or Partner die, unless they have initialed aparagraph in Section 16(a), below, authorizing the survivor to remain in the Cryo Program.

vi. If both Patient and Partner die, unless the legal representative of the last-to-die's estate notifies WCFC in writing within 90 days of the date of the last-to-die's death what use to make of the Cryopreserved Material or unless Patient and Partner have initialed a paragraph in Section 16(b), below, and then in accordance with the provisions of the selected paragraph in Section 16(b).

vii. If Patient and Partner fail to pay WCFC in accordance with the provisions of paragraph 5(a), above.

d. If Patient and Partner elect to extend the term of this Agreement, the extended term shall be for one additional year. At the end of this one year extended term, Patient and Partner must arrange for the storage of their Cryopreserved Material at a long term storage facility and arrange for the transport of the Cryopreserved Material in accordance with the provisions of Section 6, below. If Patient and Partner do not arrange for the storage and transport of their Cryopreserved Material at the end of the extended term, then WCFC shall destroy the Cryopreserved Material following standard medical laboratory procedures for elimination of bio-hazardous material. Ninety days prior to the termination of the extended term of this Agreement, WCFC will give Patient and Partner notice of the termination date of the Agreement and their two options under this paragraph—storage at another facility or destruction of the Cryopreserved Material. Under no circumstances shall the term of this Agreement extend beyond three years.

6. <u>Transport of Cryopreserved Material</u>. Patient and Partner acknowledge that WCFC, for medical reasons, recommends against the transporting of the Cryopreserved Material

for any purpose. Therefore, to the extent that it becomes necessary for the Cryopreserved Material to be transported from WCFC to any third party, Patient and Partner jointly and severally: (i) assume all risk and expense associated with the transport of the Cryopreserved Material; (ii) agree to indemnify and, if necessary, defend WCFC from all liability, costs and expenses (including any attorney fees incurred by WCFC) associated with any transport of the Cryopreserved Material; (iii) pay WCFC a laboratory transport fee in addition to WCFC's other costs and expenses; and (iv) comply with such other conditions as WCFC may in its reasonable discretion impose in order to effectuate the safe transport of the Cryopreserved Material.

7. WCFC's Right to Discontinue the Program. WCFC presently intends to operate its Cryo Program indefinately. However, WCFC reserves the right to discontinue for any reason the operation of the Cryo Program following not less than 90 days written notice to Patient and Partner. If within 90 days following notice that the Cryo Program will be terminated, Patient and Partner instruct WCFC with respect to the disposition of the Cryopreserved Material, WCFC will follow those instructions at the sole expense of Patient and Partner. If Patient or Partner do not instruct WCFC what to do with the Cryopreserved Material within 90 days after notice is given, WCFC will destroy the Cryopreserved Material following standard medical laboratory procedures for destruction of bio-hazardous material.

8. No Assurances. Patient and Partner acknowledge that the procedures involved in harvesting and fertilizing eggs and creating and implanting embryos are risky and may not lead to Patient achieving a pregnancy. Patient and Partner want to participate in the Cryo Program with full knowledge that there is no guarantee that a pregnancy will occur.

9. Frozen Embryos Involve Risks. Although laboratories worldwide now have the

ability to cryopreserve human embryos and to establish pregnancy after transfer, this does not mean that cryopreservation eliminates the normal risk of obstetric complications or fetal abnormalities, but rather that cryopreservation does not appear to create an increased risk, although the possibility of a presently unforeseen risk cannot be completely eliminated. However, while cryoperservation may not increase the risk of fetal abnormalities, it does decrease the likelihood that pregnancy will be achieved because the pregnancy rate for embryo transfers is lower with cryopreserved embryos than with newly created "fresh" embryos.

10. No Liability for Mechanical Failure. Patient and Partner understand that mechanical support system equipment failure can occur. Patient and Partner therefore acknowledge and agree that neither WCFC, nor its officers, directors, employees, or agents are liable for any destruction, damage, or improper freezing, maintenance, storage, withdrawal, thawing, or delivery caused by or resulting from any malfunction of the storage tank or laboratory instruments used to cryopreserve and maintain the Cryopreserved Material, any utility failure, strike, cessation of services or other labor disturbance, any war, act of a public enemy or other disturbance, any fire, wind, earthquake, water, or any other acts of nature, or the failure of any other laboratory which may have possession of the Cryopreserved Material. Patient and Partner specifically waive their right to sue WCFC, its officers, directors, agents or employees, in the event the embryos or eggs are lost or destroyed because of equipment failures or acts beyond the control of WCFC, either as enumerated above or otherwise.

11. No Insurance or Other Compensation. Patient and Partner understand and agree that WCFC neither has nor provides insurance coverage to compensate Patient or Partner if the embryos or eggs are harmed in any way by the cryopreservation procedure described in this

Agreement. Additionally, WCFC does provide any compensation or free medical care to Patient or Partner if the embryos or eggs are harmed in any way by the cryopreservation procedure described in this Agreement.

12. Notices. All notices required under this Agreement shall be given by certified mail, return receipt requested with a copy by regular mail postage prepaid to Patient and Partner at the address following their signature on this Agreement and to WCFC at 11160 Warner Avenue, Suite 411, Fountain Valley, CA 92708. Notice will be deemed given 3 days after the certified and regular letters are mailed with sufficient postage, whether the certified mail is signed for or not. Either party may change their mailing address by notifying the other in accordance with this section. It is the responsibility of the patient and partner to notify WCFC in writing anytime there is a change of address.

13. Further Consents. Each time Patient and Partner desire to use any of the Cryopreserved Material, both Patient and Partner must sign a written consent instructing WCFC what use to make of the material.

14. Attorney Fees. In any action or proceeding arising out of this Agreement, the prevailing party shall recover reasonable attorney fees.

15. Arbitration and Jurisdiction.

a. Any dispute arising out of this Agreement which is not resolved within 30 days after written notice, shall be first submitted to mediation before a retired judge affiliated with JAMS or Judicate West to be agreed upon by the Parties. If the mediation does not successfully resolve the dispute, the dispute shall be submitted to binding arbitration in Orange County, California in accordance with California Code of Civil Procedure § 1281, *et seq.*, before a retired

judge affiliated with JAMS or Judicate West to be agreed upon by the Parties. If the Parties cannot agree upon an mediator or arbitrator within ten days after any party requests mediation or arbitration, then the matter shall be submitted to JAMS and JAMS will select the mediator or arbitrator. The arbitrator who is selected/appointed shall have final and binding authority to make any necessary rulings, orders and awards. Any award rendered by such arbitration shall be final and binding on the Parties and judgment confirming the award may be entered thereon in the Orange County Superior Court. The parties agree that the provisions of California law applicable to health care providers shall apply to all disputes within the ambit of this agreement, including, without limitation, Code of Civil Procedure sections 340.5 and 667.7 and Civil Code sections 3333.1 and 3333.2. Any party may bring before the arbitrator a motion for summary judgment or summary adjudication in accordance with the Code of Civil Procedure section 437 (c) and the arbitrator shall have the authority to make rulings or render an award in the same manner and under the same circumstances that a sitting judge would have the authority to grant a motion a motion for summary adjudication or summary judgment. Discovery shall be conducted pursuant to Code of Civil Procedure section 1283.5. The prevailing party in any such dispute shall be entitled to recover attorney fees.

b. The Parties agree to submit to the jurisdiction of the Orange County Superior Court in any action arising out of this Agreement. Patient and Partner also understand and agree that they are waiving their right to a trial by a jury of their peers.

16. **<u>Future Disposition</u>**. Should something unexpected happen to Patient or Partner, Patient and Partner would like WCFC to process the Cryopreserved Material in accordance with their instructions set forth in this Section 16. (Please choose one option each from paragraphs a,

b and c, below. Both partners must agree upon and initial the choice for it to be effective.)

a. If either Patient or Partner should die, the Cryopreserved Material should be:

i. _____/_____ Destroyed according to WCFC's policy for destruction of
Patient/Partner

bio-hazardous material.

ii. _____/_____ Given to Partner or Patient, whichever remains alive.
Patient/Partner

iii. _____/_____ Donated to the University of California, Irvine or to
Patient/Partner

California Stem Cell, Inc. to be used to create stem cells or stem cell lines which will be used by qualified researchers in both the for-profit and not-for-profit sectors in research about human development, in testing new pharmaceuticals and, perhaps one day for therapeutic uses in humans. (This choice requires you to also sign an agreement entitled "West Coast Fertility Center Consent to Act a Human Research Subject" which will be provided to you.)

b. If both Patient and Partner die, the Cryopreserved Material should be:

i. _____/_____ Destroyed according to WCFC's policy for destruction of
Patient/Partner

bio-hazardous material.

ii. _____/_____ Donated to another infertile couple.
Patient/Partner

iii. _____/_____ Donated to the University of California, Irvine or to
Patient/Partner

California Stem Cell, Inc to be used to create stem cells or stem cell lines

which will be used by qualified researchers in both the for-profit and not-for-profit sectors in research about human development, in testing new pharmaceuticals and, perhaps one day for therapeutic uses in humans (This choice requires you to also sign an agreement entitled "West Coast Fertility Center Consent to Act a Human Research Subject" which will be provided to you.)

c. If Patient and Partner are divorced the Cryopreserved Material should be:

i. _____/_____ Destroyed according to WCFC's policy for destruction of
Patient/Partner

bio-hazardous material.

ii. _____/_____ Given to: _____
Patient/Partner

(must be either Patient or Partner)

17. **Entire Agreement.** Except for the instructions given to WCFC in the Disposition of Extra Eggs/Embryos agreement that Patient and Partner have signed with WCFC, Patient and Partner acknowledge and agree that all of their rights and duties and all of WCFC's rights and duties concerning the Cryopreserved Material are set forth in this Agreement and that there are no understandings or agreements concerning the Cryopreserved Material except as expressly set forth in this Agreement. Patient and Partner expressly represent to WCFC that they are not relying on any oral representations of WCFC, or any staff member of WCFC, concerning the Cryopreserved Material that are not set forth in this Agreement.

18. **<u>Receipt of Agreement</u>**. Patient and Partner acknowledge that they have received a signed copy of this Agreement and that this Agreement forms a binding contract among Patient and Partner and WCFC.

Dated: _____

_____
Patient Signature

_____
(Print Name)

_____
(Address for Notice Purposes)

_____
Partner Signature

_____
(Print Name)

_____
(Address for Notice Purposes)

Dated: _____

_____
W.C.F.C. Representative Signature

_____
(Print Name)

To: Ken Berger <ken@californiastemcell.com>

——— Forwarded message ———
From: "Antoine La" <tlsss@aol.com>
Date: Apr 27, 2012 11:46 AM
Subject: Re: Some paperwork needed
To: <gabriel@californiastemcell.com>

Hello Gabriel,
How are you? This is the blank Cryo agreement. Please call if you have any question. Thanks.

Antoine La, ELD, EMB
Embryology Lab. Director
West Coast Fertility Centers
11160 Warner Ave Suite 411
Fountain Valley, CA 92708
www.eggfreezing.com
www.ivfbaby.com
Office: 714-513-1399 X 108
Cell : 714-394-3145

—Original Message—
From: Gabriel Nistor <gabriel@californiastemcell.com>
To: Antoine La <Tlsss@aol.com>
Cc: ken <ken@californiastemcell.com>
Sent: Mon, Apr 23, 2012 11:57 am
Subject: Some paperwork needed

Hi Antoine,

[redacted]

Recently we had a request from a review committee to provide documentation to the embryo's we used to generate stem cell lines. They are asking for a blank or redacted copy of the "Cryopreservation Program Participation Agreement" that is referenced on page 1 of the embryo donation consent. For information, the embryos and documents that we obtained from this donor are referenced by cycle number 05-03-1593 dated 9/16/05, therefore the document version should be before or around that date if you can kindly send me a blank or a redacted copy of original (with the HIPAA information blanked). I copied this e-mail to our head of QA department, Dr. Ken Berger, who is in direct contact with the reviewing authority requesting this document.

Thank you in advance and with best regards,

Gabriel

[redacted]