Guide to Submission

GENEA

Submission #2012-ACD-002

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NOTE: Other reference documents (e.g. legislation, guidelines, etc.) provided by the submitter are not included as they were not utilized for the review.

hESC Registry Application Database
Detailed Listing for Request #: 2012-ACD-002
May 7, 2012

hESC Registry Application Search Results

Request #: 2012-ACD-002
Status: Pending

Review: ACD

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

Cell Lines: 3
Available: 3

Previous #:
2011-DRAFT-016
2011-ADM-021

Email
Edit
Delete
Switch to ADM

Organization: GENEA
Org Address: Level 2, 321 Kent Street Sydney NSW 2000 AUSTRALIA
DUNS: 750354490 **Grant Number(s):**
Signing Official (SO): Tomas Stojanov / +61-2-84846505 / tomas.stojanov@genea.com.au
Submitter of Request: Julia Schaft / +61-2-92296449 / julia.schaft@genea.com.au
Submitter Comments: Please note that our company name has changed from Sydney IVF to Genea in 2011. Some references in our supporting documents are to the old company name.

Line #1: GENEA017
NIH Approval #:
Available: Yes
Embryo from U.S.: No
Embryo Donated in Year(s): 2007
Provider Name: GENEA
Provider Phone:
Provider Email: julia.schaft@genea.com.au
Provider URL:
Provider Restrictions: Subject to individual terms and conditions. Please contact us for more information

NIH Restrictions:

Additional Information: From embryo affected by Huntington's Disease

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Line #2: GENEA041
NIH Approval #:
Available: Yes
Embryo from U.S.: No
Embryo Donated in Year(s): 2007
Provider Name: GENEA
Provider Phone:
Provider Email: julia.schaft@genea.com.au
Provider URL:
Provider Restrictions: Subject to individual terms and conditions. Please contact us for more information

NIH Restrictions:

Additional Information: From embryo affected by Cystic Fibrosis

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Line #3: GENEA068
NIH Approval #:
Available: Yes
Embryo from U.S.: No
Embryo Donated in Year(s): 2007
Provider Name: GENEA
Provider Phone:
Provider Email: julia.schaft@genea.com.au
Provider URL:

Provider Restrictions: Subject to individual terms and conditions. Please contact us for more information

NIH Restrictions:

Additional Information: From embryo affected by Wilm's Tumour

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Supporting Documents:
Document 1: (PDF - 12/15/2011) Assurance Letter and Business Name Registration - Elements: 16
Document 2: (PDF - 12/15/2011) Summary of Supporting Documents - Elements: 16
Document 3: (PDF - 12/15/2011) Overview of the Derivation Process - Elements: 16
Document 4: (PDF - 12/15/2011) Mapping of the Elements - Elements: 16
Document 5: (PDF - 12/15/2011) ISO Consent Forms - Elements: 1,2,3,4,5,7,8,9,10,11,12,13,14,15
Document 6: (PDF - 12/15/2011) HREC Approval - Elements: 16
Document 7: (PDF - 12/15/2011) Publications - Elements: 16
Document 8: (PDF - 12/15/2011) Assurance Letter - Elements: 1,2,5,6,8
Document 9: (PDF - 12/15/2011) Regulatory Documents - Elements: 1,2,3,4,5,6,7,8,9,10,11,14

Administrative Comments: SO certifications updated E. Gadbois 13 Feb 2012

Added Genetic Disease Mutation information for each line - by DHannemann 08 Mar 2012

Decision Memo signed by SLandis - by DHannemann 26 Apr 2012

IIB Assurance - by DHannemann 03 May 2012

redundant emails deleted by E. Gadbois 7 May 2012

Administrative Attachments:

Document 2: (PDF - 02/13/2012) Updated SO Certification 9 Feb 2012 email
Document 3: (PDF - 02/13/2012) training manual 9 Feb 2012 email
Document 4: (PDF - 02/13/2012) withdrawal form 9 Feb 2012 email
Document 6: (PDF - 02/24/2012) Response from GENEA 22 Feb 2012
Document 7: (PDF - 04/27/2012) Decision Memo signed by SLandis
Document 8: (PDF - 05/03/2012) IIB Assurance

Status History:
Draft: 12/13/2011
Pending: 12/18/2011

Emails Sent: 12/18/2011-New_Applicaton_Email

Previous ADM Request Number: 2011-ADM-021
Switched from ADM to ACD Date: 05/01/2012
Reason for Switch to ACD Review:
Per 4/30/2012 email correspondence with submitter (revised assurance pending due to technical issue)-E. Gadbois

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Added By: Commons\T.Stojanov **On:** 12/13/2011 | **Last Updated By:** NIH\gadboisel **On:** 05/07/2012 | **Record ID:** 86

Document 2:
Summary of Supporting Information for disease specific PGD cell lines (protocol 309710)

DOCUMENT 1:

This document contains the NIH Section II(B) Assurance letter and the Change of Business Name disclaimer.

DOCUMENT 2:

This document (current) provides a description of each of the attached documents within each hESC bundle.

DOCUMENT 3:

This document provides an overview of the Genea stem cell line derivation process.

Document 4:

This document contains the mapping of Elements of Section II (A) of the July 7, 2009 NIH Guidelines on Human Stem Cell Research, to the documents provided.

DOCUMENT 5:

This document contains collated ISO consent forms. Consent forms used for the stem cell derivation consent process at Genea are controlled ISO documents. Over a period of time a number of different ISO versions of consent forms were in use. Controlled blank versions of the consent forms signed by the donors are included in Document 5. The various stem cell lines were grouped into different bundles based on the version of the consent forms that were signed. The redacted originally signed forms can be supplied upon request.

For more information on the consent process please refer to Document 3

DOCUMENT 6:

This document contains a letter for the Ethics Committee Approval of the Development of Human Embryonic Stem Cells and Commercial Use of Embryonic Stem Cell Lines.

For more details on the Ethics approval process, please refer to document 3.

DOCUMENT 7:

This document contains the publications that have reference to the stem cell lines.

DOCUMENT 8:

This document contains an assurance letter signed by both the medical director and the CEO of Genea, stating there is a clear separation between clinical and research roles in the project, and that donors are allowed to withdraw their consent for research up until the embryo is actually used.

DOCUMENT 9: "Regulatory documents: Copy of License 309710, and relevant Australian guidelines and legislation"

This document contains the following:

- NHMRC licence for the 309710 protocol (allowing us to derive hESC lines from disease specific PGD embryos).
- NHMRC information kit, detailing requirements for embryo research licence applications and maintenance.
- Research Involving Human Embryos Act
- Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research
- National Statement on Ethical Conduct in Human Research

Consent and derivation process for embryonic stem cell lines GENEA017, GENEA041 and GENEA068.

Overview of the Australian embryo research licensing process

All human embryo research in Australia is subject to regulation through the Research involving human embryos Act 2002. Under this Act research involving human embryos can only be performed if authorised by the National Health and Medical Research Council (NHMRC) through a specific research licence. Human Research Ethics Committee (HREC) approval is a prerequisite for every licence application and each subsequent variation of the licence. The NHMRC licensing Committee is reviewing each application on the basis of compliance with the Act, the Ethical Guidelines on the use of assisted reproductive technology in clinical practice and research and the National Statement on Ethical Conduct in Human Research. After a licence is granted, regular inspections and reporting processes guarantee that licence conditions are strictly adhered to.

HREC approval for the project "Derivation of human embryonic stem cells from embryos identified through pre-implantation genetic diagnosis to be affected by known serious monogenic conditions" was first obtained in 2005. The licence application was made to the NHMRC and subsequently granted in 2007 (Australian embryo research licence 309710).

Written ethics approval was not prepared at the time of review in 2005, but rather communicated as a result of the meeting and documented in meeting minutes. In October 2009, a retrospective statement was prepared on behalf of the Ethics Committee, explaining that the process of deriving stem cells (protocol 309710), including all associated consent forms and participant information packages were approved at that time.

All changes to consent forms/participant info have been approved by the HREC.

The NHMRC can elect to review consent form changes and has reviewed some changes, as evidenced by license revisions

Overview of the derivation of GENEA017, GENEA041 and GENEA068

GENEA017, GENEA041 and GENEA068 are derived from frozen embryos, identified as affected after Pre-implantation Genetic Diagnosis (PGD).

It is routine practice at Genea that embryos identified as affected after PGD are frozen for periodically undertaken subsequent confirmation of the PGD result as part of our quality assurance program. This practice is performed in accordance with clinical guidelines (ESHRE and PGDIS) and also enables us to seek consent from patients for the derivation of hESC

lines from their frozen affected embryos as not all embryos are needed to cover clinical requirements for confirmation testing.

Consent for the derivation of GENEA017, GENEA041 and GENEA068 is separated into two distinct stages. Each stage is completed with the signing of a specific form. The purpose of each of the two stages and consent forms is described below. (Please note that all consent forms are provided to the patients in English. Translation services (if required) are provided as part of Genea clinical patient support services):

1. Declaration of Excess PGD Embryos consent form (PGD DOEE): At this stage donors are declaring that the affected embryos are excess to their clinical needs.
2. Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition Consent Form and Participant Information: At this stage donors are consenting for the derivation of embryonic cell lines from their affected excess embryos

Consent for stem cell derivation can only be given after the DOEE has been signed (stage 1). Stem cell derivation and subsequent distribution and use of the cell line outside of Genea can only occur after specific consent forms have been signed (stage 2).

After signing consent for stem cell derivation, patients donating frozen affected embryos have a cooling off period of 14 days during which consent can be withdrawn at any stage. Embryos will not be used for stem cell derivation until the cooling off period has expired.

It is Genea policy to allow the donors to withdraw their consent for research until the embryo is actually used. Even after their embryos have been entered into the research protocol, and up until the point a potentially created cell line is distributed outside of Genea, consent can be withdrawn. Embryos may not be intact, but any remnants will then be discarded according to patient's wishes (see Assurance Letter-Document 8).

Consent forms used for the stem cell derivation consent process at Genea are controlled ISO documents. Over a period of time a number of different ISO versions of consent forms were in use. Controlled blank versions of the consent forms signed by the donors at the time of consent are included in Document 5. Redacted originally signed forms can be supplied upon request.

Table 1 below summarises dates of embryo creation (or oocyte pick up – OPU), consent signing and cell line derivation for GENEA017, GENEA041 and GENEA068.

Table 1: Summary of Dates

	GENEA017	GENEA041	GENEA068
EMBRYO FORMATION (OPU) DATE	01-SEP-06	23-MAR-07	09-MAY-07
DECLARATION OF EXCESS PGD EMBRYOS (VERSION 11/05/07)-DATE SIGNED	17-MAY-07	25-MAY-07	08-JUN-07
CONSENT FORM 309710 (VERSION 11/05/07) -DATE SIGNED	17-MAY-07	25-MAY-07	08-JUN-07
CELL LINE DERIVATION DATE	27-JUNE-07	14-JAN-09	03-NOV-10

GENEA017, GENEA041 and GENEA068:

Mapping of the Elements of Section IIA

Within the consent forms and associated participant information brochures, the elements listed in Section IIA of the July 7, 2009 NIH Guidelines on Human Stem Cell Research can be mapped to the various consents as follows: (please note that sections quoted are specific to the ISO versions of the forms originally signed by the donors at the time of use)

Controlled blank versions of the consent forms signed by the donors at the time of use are included in Document 5. Redacted de-identified originally signed forms can be supplied upon request. The couples who donated embryos for GENEA017, GENEA041, and GENEA068 did not use donor sperm or eggs. All stages of consent have been signed by all responsible people ie. Embryo mother and father.

The individual elements are also addressed by referencing specific sections from regulatory documents describing Australian guidelines and legislation for human embryo research. Only under these conditions has Genea obtained licences for human stem cell derivation (licences 309703 and 309710); compliance with this framework is continually monitored for full compliance since the licences have been issued.

Element 1: hESCs were derived from human embryos that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose.

> **Declaration of Excess PGD Embryos**—"We declare that the embryos produced from our eggs and sperm on [date of OPU] for the purpose of pre-implantation genetic diagnosis (PGD) are excess to our reproductive needs."
>
> **RIHE Act 2002 section 11** – Defines an offense against the Act as using an embryo that is not an excess ART embryo.
>
> **RIHE Act 2002 section 9** – Defines "excess ART embryo"

Element 2: hESCs were derived from human embryos that were donated by individuals who sought reproductive treatment (donor(s)) and who gave voluntary written consent for the human embryos to be used for research purposes.

> As required by Australia's "Research Involving Human Embryos Act 2002", consent specific for Embryo Research Protocol 309710 was obtained from all responsible persons in the following informed consent forms:

1. **Declaration of Excess PGD Embryos Consent Form (PGD DOEE)**
2. **Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition Licensed Embryo Research Protocol 309710Participant Consent Form**

Declaration of Excess PGD Embryos

B. "We are prepared to consider donating our excess embryos which are found to be GENETICALLY ABNORMAL (AFFECTED) and not suitable for transfer, for use in ethically approved and licensed scientific studies. Please provide us with details of proposed projects. If we decide to donate our embryos to research we understand that we will be required to sign forms giving our consent to specific projects (licensed embryo research protocol 309710)."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

- Paragraph 2: "We freely choose to take part in this project...."
- Paragraph 6: "We hereby agree that our embryos produced on [date] carrying a genetic condition may be used in this research study."

RIHE Act 2002 section 9 – meaning of excess ART embryo

National statement on ethical conduct in human research Chapter 2.2 – Describes general requirements for consent

Element 3: All options available in the health care facility where treatment was sought pertaining to the embryos no longer needed for reproductive purposes were explained to the individual(s) who sought reproductive treatment.

Declaration of Excess PGD Embryos—"We have been offered an opportunity to discuss our options with a counselor, and;
(Please circle the appropriate paragraph)

A. We hereby request that they be allowed to succumb. We do not consent to any scientific studies on our embryos before they are allowed to succumb, or;
B. We are prepared to consider donating our excess embryos which are found to be GENETICALLY ABNORMAL (AFFECTED) and not suitable for transfer, for use in ethically approved and licensed scientific studies. Please provide us with details of proposed projects. If we decide to donate our embryos to research we understand that we will be required to sign forms giving our consent to specific projects (licensed embryo research protocol 309710).

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 13: " ...if you would like to discuss your embryos (and the options you have with them) more generally with a Sydney IVF counsellor not associated with the research projects, please phone Evelyn Zwahlen or any of our IVF counsellors on 9229 6420."

National statement on ethical conduct in human research Chapter 2.2 – Describes general requirements for consent

Please note: It is Genea clinical policy that embryos identified as affected by the genetic condition tested for in the PGD department, cannot be used for clinical embryo transfer. Donation of affected embryos to another couple is not desirable or possible. The only options for embryos found to be affected by a genetic condition is to be discarded or to be used (either fresh or after cryopreservation) for research purposes (refer to Document 8).

Element 4: No payments, cash or in kind, were offered for the donated embryos.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 9:"Under Australian Legislation money is not attributable or payable to the donor of the embryo or embryos from which the cells are derived and it is illegal for embryos to be bought or sold."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 4: "We acknowledge that Sydney IVF may receive a commercial payment from making stem cells available to others. We acknowledge this payment is for the value added from the derivation and testing process and, potentially, the ongoing help Sydney IVF provides another laboratory in further developing or tailoring the cells for that organization's particular research and development program and that we have no claim on any potential payments resulting from the use of our embryos. We understand that we are altruistically donating our embryos for research and development purposes without any restriction or direction regarding the use to which created stem cell lines may be put."

National statement on ethical conduct in human research Chapter 2.2 – Describes general requirements for consent

Element 5: Policies and/or procedure were in place at the health care facility where the embryos were donated that neither consenting nor refusing to donate embryos for research would affect the quality of care provided to potential donor(s).

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 10: "You do not have to take part in this project. Your participation is entirely voluntary."

Paragraph 11: "Whatever your decision, it will not affect your medical treatment or your ongoing professional relationship with medical, nursing or embryology staff at Sydney IVF, should this still be relevant to you."

Paragraph 16: "Should at any time you have concerns or complaints about the conduct of the study you can contact the Secretary to the Ethics Committee, Dr Lindsay Gillan, on 8484 6506, or the Chairman of the Ethics Committee, Rev'd Dr Ivan Head on 9550 7444."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 2: "We freely choose to take part in this project and understand that we can withdraw our consent without prejudicing our medical treatment or our ongoing professional relationship with medical, nursing or embryology staff at Sydney IVF, should this still be relevant to us."

Paragraph 5: "We have been informed that should we have concerns or complaints about the conduct of the study we can contact the Secretary to the Sydney IVF Ethics Committee Dr Lindsay Gillan (on 8484 6506) or the Chairman of the Committee, Rev'd Dr Ivan Head (on 9550 7444)."

National statement on ethical conduct in human research Chapter 2.2 – Describes general requirements for consent

Please note: Document 8 confirms that research staff is not involved in the clinical care of the patient and that clinical staff is not involved in the research project at any stage. Doctors are not made aware of the research consent status at any stage of the treatment.

Element 6: Decisions related to the creation of human embryos for reproductive purposes should have been made free from the influence of researchers proposing to derive or utilize hESCs in research. The attending physician responsible for reproductive clinical care and the researcher deriving and/or proposing to utilize hESCs should not have been the same person unless separation was not practicable.

Signing of the Declaration of Excess Embryos and specific consent forms occurred after the creation of the embryos for reproductive purposes (see Table 1 of

Document 3 for IVF dates and signing of "Declaration of Excess Embryos Form" dates).

The project was performed with a clear separation between clinical and research roles: The treating clinicians were in no way involved in cell line derivation. Researchers were not involved in the clinical care of the patients or the embryo consenting process. Please refer to Document 8, Letter of Assurance, from GENEA.

Ethical guidelines on the use of ART in clinical practice and research, section 17.16 – Requirement and guidelines for obtaining proper consent

Element 7: At the time of donation, consent for that donation should have been obtained from the individual(s) who had sought reproductive treatment. That is, even if potential donor(s) had given prior indication of their intent to donate to research any embryos that remained after reproductive treatment, consent for the donation for research purposes should have been given at the time of the donation.

As required by Australia's "Research Involving Human Embryos Act 2002", consent specific for Embryo Research Protocol 309710 was obtained from all responsible persons in the following informed consent forms:

1. Declaration of Excess PGD Embryos form (PGD DOEE)
2. Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition consent form.

Signing of the Declaration of Excess PGD Embryos and specific consent forms occurred after the creation of the embryos for reproductive purposes (see Table 1 of Document 3 for IVF dates and signing of "Declaration of Excess PGD Embryos Consent Form" dates).

Element 8: Donor(s) should have been informed that they retained the right to withdraw consent until the embryos were actually used to derive embryonic stem cells or until information that could identify the donor(s) was no longer retained by the researchers, if applicable.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 10: "If you do decide to donate your embryos affected by a genetic condition they will be cryostored ("frozen") for at least two weeks before use. You can withdraw your consent at any time during this two weeks period."

Paragraph 11: "Because embryos are destroyed in the research project (as opposed to the embryos succumbing naturally) this is a moral concern for some people. It is

for this reason that embryos will not be used for at least two weeks after you have given your consent, which gives you this time to reconsider your decision."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 2: "We freely choose to take part in this project and understand that we can withdraw our consent without prejudicing our medical treatment or our ongoing professional relationship with medical, nursing or embryology staff at Sydney IVF, should this still be relevant to us. Because the process of deriving embryonic stem cells will destroy our embryos, Sydney IVF will not use our embryos until 2 weeks after we give our consent, in case we decide to withdraw our consent."

Please note: It is Genea policy to allow the donors to withdraw their consent for research until the embryo is actually used. Even after their embryos have been entered into the research protocol, and up until the point a potentially created cell line is distributed outside of Genea can consent be withdrawn. Embryos may not be intact, but any remnants will then be discarded according to patient's wishes (refer to Document 8).

Ethical guidelines on the use of ART in clinical practice and research, Section 17.19 – Requirement to allow for withdrawal of consent

Element 9: During the consent process the donor(s) were informed that the embryos would be used to derive hESCs for research.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 1: "The aim of this project is to produce human embryonic stem cell (hESC) lines for research efforts to study diseases linked with specific genetic or chromosomal anomalies.

Paragraph 2: "We ask your consent to attempt to derive stem cells from your embryos that have been identified as affected by a GENETIC condition by PGD."

Paragraph 5: "Please note that producing stem cells from embryos will destroy the embryos"

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 2: "...Because the process of deriving embryonic stem cells will destroy our embryos, ..."

Ethical guidelines on the use of ART in clinical practice and research, Section 17.18 –Requirement to provide all relevant information

Element 10: During the consent process the donor(s) were informed of what would happen to the embryos in the derivation of hESCs for research

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 5: "We will isolate cells from the embryos, generally at the stage of blastocysts. Please note that producing stem cells from embryos will destroy the embryos."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 2: "...Because the process of deriving embryonic stem cells will destroy our embryos, ..."

Ethical guidelines on the use of ART in clinical practice and research, Section 17.18 –Requirement to provide all relevant information

Element 11: During the consent process the donor(s) were informed that hESCs derived from the embryos might be kept for many years.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 3: "Should your embryo or embryos appear to produce a "stem cell line" (which means that the cells show the potential of multiplying themselves in the laboratory for an indefinite period) we would like to make the stem cells available to researchers within and outside Sydney IVF for further research into the genetic condition or conditions that are affecting your embryos."

Ethical guidelines on the use of ART in clinical practice and research, Section 17.18 –Requirement to provide all relevant information

Element 12: During the consent process the donor(s) were informed that the donation was made without any restriction or direction regarding the individual(s) who may receive medical benefit from the use of the hESCs, such as who may be the recipients of transplants of the cells.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 8: "While this project is not likely to benefit you directly in the immediate future, we intend that this research will advance medical knowledge and we hope to improve the treatment of patients in the future who suffer from the effects of the gene mutations we uncover with PGD. In the long term, it is plausible that people with the genetic condition affecting your embryos could benefit from the research into drug development."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 4: "We understand that we are altruistically donating our embryos for research and development purposes without any restriction or direction regarding the use to which created stem cell lines may be put."

Element 13: During the consent process the donor(s) were informed that the research was not intended to provide direct medical benefit to the donor(s).

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 8: "While this project is not likely to benefit you directly in the immediate future, we intend that this research will advance medical knowledge and we hope to improve the treatment of patients in the future who suffer from the effects of the gene mutations we uncover with PGD. In the long term, it is plausible that people with the genetic condition affecting your embryos could benefit from the research into drug development."

Element 14: During the consent process the donor(s) were informed that the results of research using the hESCs may have commercial potential, and that the donor(s) would not receive financial or any other benefits from any such commercial development.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 9: "There are a number of companies or institutions Sydney IVF is working with, or intends to work with, and these include commercial organizations as well as non-profit organizations. In this respect, we should also point out that Sydney IVF may receive a commercial payment from making stem cells available to others. This payment is for the value added from the derivation and testing processes that lead to the stem cell line and, potentially, any ongoing help Sydney IVF provides another laboratory in further developing or tailoring the cells for that organization's particular research and development program. Under Australian Legislation money is not attributable or payable to the donor of the embryo or embryos from which the cells are derived and it is illegal for embryos to be bought or sold."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 4: "We acknowledge that Sydney IVF may receive a commercial payment from making stem cells available to others. We acknowledge this payment is for the value added from the derivation and testing process and, potentially, the ongoing help Sydney IVF provides another laboratory in further developing or tailoring the cells for that organization's particular research and development program and that we have no claim on any potential payments resulting from the use of our embryos.

Ethical guidelines on the use of ART in clinical practice and research, Section 17.18 – Requirement to provide all relevant information

Element 15: During the consent process the donor(s) were informed information that could identify the donor(s) would not be available to researchers.

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Participant Information

Paragraph 7: "All aspects of these studies, including results, will be strictly confidential and only the investigators named above and the embryologists responsible for the laboratory procedures involving your embryos will have access to information on participants. However, inspectors appointed by the *Embryo Research Licensing Committee* of the NHMRC can require access to your records for auditing purposes to ensure Sydney IVF meets the requirements of the *Research Involving Human Embryos Act 2002*. Reports of our studies are likely to be submitted for publication, but individual participants will not be identifiable in such reports. Of course you can yourself discuss the project and your involvement in it with anyone you wish (the research itself is not a secret)."

Research Project Involving Human Embryonic Stem Cells Generated From Embryos Diagnosed By PGD As Having A Genetic Condition-Consent Form

Paragraph 3: "We understand that Sydney IVF will keep our taking part in the research study strictly confidential and that we will not be identified. However, we also understand that inspectors appointed by the Embryo Research Licensing Committee of the NHMRC may require access to our records and the outcomes of this research will be reported to the NHMRC Licensing Committee."

Please note: Access to linking information between the stem cell line and the embryo donor is strictly limited to embryology staff and the Genea scientists involved in the stem cell project. While information about the participants like the absence of infectious diseases might have been communicated, at no stage was the identity of the donors revealed to anyone outside of Genea. All our consent forms are de-identified, the cell line identifier does not contain patient information. Linking

information is only retrievable through the research database to which access is actively restricted"

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Document 5

SYDNEY IVF

DECLARATION OF EXCESS PGD EMBRYOS

I, _____
First Name Second Name Surname

Date of Birth _____

of _____

_____ Post Code _____

and I, _____
First Name Second Name Surname

Date of Birth _____

of _____

_____ Post Code _____

We declare that the embryos produced from our eggs and sperm on SIVF to insert date for the purpose of preimplantation genetic diagnosis (PGD) are excess to our reproductive needs. We have been offered an opportunity to discuss our options with a counsellor, *and;*
(Please circle the appropriate paragraph)

A. We hereby request that they be allowed to succumb. We do not consent to any scientific studies on our embryos before they are allowed to succumb, *or;*

B. We are prepared to consider donating our excess embryos which are found to be GENETICALLY ABNORMAL (AFFECTED) and not suitable for transfer, for use in ethically approved and licensed scientific studies. Please provide us with details of proposed projects. If we decide to donate our embryos to research we understand that we will be required to sign forms giving our consent to specific projects (licensed embryo research protocol 309710)

Signed: _____ Date: _____

Signed: _____ Date: _____

Witness: _____ Date: _____

OFFICE USE ONLY

Embryo details/signatures checked by: _____ *Date:* _____

Embryos discarded *Date:* _____ *By:* _____ _____

OR

Embryos allocated to research *Date:* _____ *By:* _____ _____

SYDNEY IVF

RESEARCH PROJECT INVOLVING HUMAN EMBRYONIC STEM CELLS GENERATED FROM EMBRYOS DIAGNOSED BY PGD AS HAVING A GENETIC CONDITION

[LICENSED EMBRYO RESEARCH PROTOCOL 309710]

PARTICIPANT INFORMATION

The aim of this project is to produce human embryonic stem cell (hESC) lines for research efforts to study diseases linked with specific genetic or chromosomal anomalies.

Comment [A1]: Paragraph 1

We ask your consent to attempt to derive stem cells from your embryos that have been identified as affected by a GENETIC condition by PGD.

Comment [A2]: Paragraph 2

Should your embryo or embryos appear to produce a "stem cell line" (which means that the cells show the potential of multiplying themselves in the laboratory for an indefinite period) we would like to make the stem cells available to researchers within and outside Sydney IVF for further research into the genetic condition or conditions that are affecting your embryos.

Comment [A3]: Paragraph 3

Our Director of Embryology (Dr Kylie De Boer), Director of Research (Dr Tomas Stojanov), Chief Scientific Officer (Dr Cynthia Roberts) and the Medical Director (Professor Robert Jansen) are conducting the study together with researchers from other institutions who wish to develop new treatments for genetic diseases. Please note that Sydney IVF and/or these collaborating institutions may profit from these activities.

Comment [A4]: Paragraph 4

We will isolate cells from the embryos, generally at the stage of blastocysts. Please note that producing stem cells from embryos will destroy the embryos.

Comment [A5]: Paragraph 5

The aim is to turn the stem cells into tissue-like cells and develop new ways of understanding and treating serious diseases. Embryonic stem cell lines carrying naturally occurring genetic mutations or specific combinations of genes offer an important tool for studying genetic controls and molecular events occurring during cell and tissue development. These lines can also be used in drug development studies to study a new drug's effects on gene expression and drug toxicity testing, including screening new drugs for activity against the atypical expression of genes that underlies genetic diseases, potentially including the disease in your family for which you are having your embryos tested.

Comment [A6]: Paragraph 6

All aspects of these studies, including results, will be strictly confidential and only the investigators named above and the embryologists responsible for the laboratory procedures involving your embryos will have access to information on participants. However, inspectors appointed by the *Embryo Research Licensing Committee* of the NHMRC can require access to your records for auditing purposes to ensure Sydney IVF meets the requirements of the *Research Involving Human Embryos Act 2002*. Reports of our studies are likely to be submitted for publication, but individual participants will not be identifiable in such reports. Of course you can yourself discuss the project and your involvement in it with anyone you wish (the research itself is not a secret).

Comment [A7]: Paragraph 7

While this project is not likely to benefit you directly in the immediate future, we intend that this research will advance medical knowledge and we hope to improve the treatment of patients in the future who suffer from the effects of the gene mutations we uncover with

Comment [A8]: Paragraph 8

PGD. In the long term, it is plausible that people with the genetic condition affecting your embryos could benefit from the research into drug development.

There are a number of companies or institutions Sydney IVF is working with, or intends to work with, and these include commercial organizations as well as non-profit organizations. In this respect, we should also point out that Sydney IVF may receive a commercial payment from making stem cells available to others. This payment is for the value added from the derivation and testing processes that lead to the stem cell line and, potentially, any ongoing help Sydney IVF provides another laboratory in further developing or tailoring the cells for that organization's particular research and development program. Under Australian Legislation money is not attributable or payable to the donor of the embryo or embryos from which the cells are derived and it is illegal for embryos to be bought or sold.

Comment [A9]: Paragraph 9

You do not have to take part in this project. Your participation is entirely voluntary. If you do decide to donate your embryos affected by a genetic condition they will be cryostored ("frozen") for at least two weeks before use. You can withdraw your consent at any time during this two weeks period.

Comment [A10]: Paragraph10

Whatever your decision, it will not affect your medical treatment or your ongoing professional relationship with medical, nursing or embryology staff at Sydney IVF, should this still be relevant to you. Because embryos are destroyed in the research project (as opposed to the embryos succumbing naturally) this is a moral concern for some people. It is for this reason that embryos will not be used for at least two weeks after you have given your consent, which gives you this time to reconsider your decision.

Comment [A11]: Paragraph 11

If you wish to obtain more information about the progress of the project and know more about the involvement of your donated embryos please contact Director of Research (Tomas Stojanov) on 9229 6420. However, not all embryos consented to a specific project(s) may necessarily be used, depending on the requirements of the research. In that case we may contact you again with other research options at Sydney IVF.

Comment [A12]: Paragraph 12

If you would like to know more at this stage, please phone our Research Nurse, Didi Bower or the Director of Embryology, Kylie de Boer on 9229 6420 (or, if you can't get on to them, ask for one of the research nurses) – or the Medical Director, Robert Jansen on 9229 6491. We would be happy to discuss the study further with you and meet with you if you would like. Alternatively, if you would like to discuss your embryos (and the options you have with them) more generally with a Sydney IVF counsellor not associated with the research projects, please phone Evelyn Zwahlen or any of our IVF counsellors on 9229 6420.

Comment [A13]: Paragraph 13

We understand this might be a difficult decision for you. One of our nurses will speak with you in the next few days to discuss the project and to answer any questions you have.

Comment [A14]: Paragraph 14

The Ethics Committee at Sydney IVF has approved this study and the research has been licensed under the *Research Involving Human Embryos Act 2002* (Licence no. 309710).

Comment [A15]: Paragraph 15

Should at any time you have concerns or complaints about the conduct of the study you can contact the Secretary to the Ethics Committee, Dr Lindsay Gillan, on 8484 6506, or the Chairman of the Ethics Committee, Rev'd Dr Ivan Head, on 9550 7444.

Comment [A16]: Paragraph 16

Enclosure: Glossary of terms; Participant consent form

SYDNEY IVF

EMBRYO RESEARCH AND STEM CELL DEVELOPMENT

GLOSSARY OF TERMS

Blastocyst: Stage of development of the *embryo* in which a fluid-filled cavity forms in the formerly **solid ball of cells (the 'morula'), about 5 days after fertilization. For the first** time, a distinction can be made between a sheet of cells to one side, which will form the embryo proper (the *inner cell mass*), and the remaining, peripheral cells, which – after **the blastocyst 'hatches' through the** *zona pellucida* and undergoes implantation – will **form the placenta (the "trophectoderm").**

DEVELOPMENTALLY Unsuitable Blastocyst (Embryo): Unsuitable for embryo transfer and implantation because of failure to grow. This is apparent because of failure to divide **("cleave") or to form a blastocyst** normally, which means that the blastocyst or earlier-stage embryo is not suitable for biopsy or transfer, and is not suitable for freezing, owing to the high likelihood of failure of the *inner cell mass* to survive [ie. embryos that would normally be discarded and, therefore by definition, be excess to reproductive need].

Affected by a GENETIC condition Blastocyst (Embryo): Carrying a genetic mutation as determined by preimplantation genetic diagnosis.

Cytoplasm: The part of a cell that is not the *nucleus* (the nucleus contains the chromosomes). The **cytoplasm is contained by the cell's 'plasma membrane' and contains all the other** cellular structures, including the *mitochondria*. Genetic inheritance is mostly by way of the nucleus (with a contribution from mother and father); a small part is by way of the **cytoplasm (with a contribution only from the mother). It's the cytoplasm of the egg into which a sperm cell is injected in the process of 'intracytoplasmic sperm insertion' (ICSI).**

Egg or Ovum (pl. *ova*): The female sex cell, or egg, from the earliest stage, through its release from the follicle (ovulation), and (to professional embryologists) through fertilization up to and sometimes beyond the stage of implantation.

Embryo: The word is used loosely to describe everything from a fertilized egg to a fetus. What many people nowadays call the embryo has for long been called the *ovum* by professional embryologists. Up to the time that the embryo would normally implant in the uterus (as a *blastocyst*), any of the cells of the fertilized ovum can develop into a whole new embryo - **they are 'totipotent'. After implantation a group of cells (the** *inner cell mass*) differentiates to form the embryo itself (later the fetus), whereas remaining **cells go on to form 'afterbirth' tissues, namely the pregnancy membranes and placenta.**

Embryonic disc: Derived from the *inner cell mass*. The part of the implanted embryo that will form the embryo itself, i.e. the *fetus*.

Inner cell mass: The inner part of the *blastocyst*, which will form the *embryonic disc*. Cells from the inner cell mass give rise to all the different types of cells in the embryo, through transformation into embryonic *stem cells*.

Stem cell: A cell in the embryo, child or adult capable of dividing repeatedly without itself aging appreciably, and retaining the ability to form different types of tissues depending on local circumstances. Embryonic stem cells form normally in the embryonic disc. Fully **formed tissues also contain stem cells, but such "adult stem cells" are** perhaps a little **more "committed" to forming tissues of a restricted range. Researchers are interested** in both forms of stem cells for possible future treatments of degenerative diseases such **as diabetes, Alzheimer's disease, Parkinson's disease and many** others, as well as cells to replace tissues or organs destroyed by cancer or cancer treatment.

SYDNEY IVF

Embryo Development

321 Kent Street
Sydney 2000

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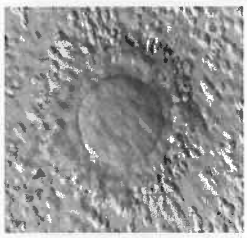
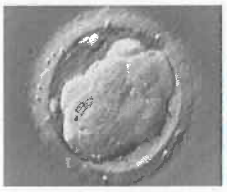
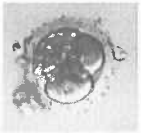
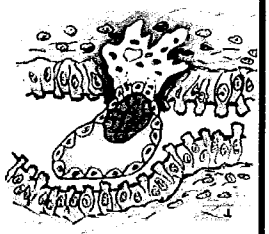
www.sydneyivf.com

egg, or unfertilized ovum		About 7 million eggs form before birth, and ~300,000 are present when periods **start. All but about 1000 are** used by menopause, an average rate of 700 per month. Only one egg is released each month, but between 2 and 30 eggs have a chance of ovulating **(depending on age) and can** be encouraged to do so in an IVF treatment.
fertilized ovum at 1 day **= pronuclear-stage embryo**		The genetic material (chromosomes) from the sperm and egg are still separate, but are about to **unite ("syngamy").**
3 day embryo (6 to 8 cells) **= cleavage-stage embryo**		Each cell could be capable **of producing a new embryo (the cells are "totipotent").** **However, "egg genes" alone can bring the embryo to this point, and more than half of** all embryos do not progress further.
4-5 day embryo (16-32 cells) **= compacting morula**		**The cells have "compacted"** to form a tissue and are no longer distinct. Compaction can happen in embryos that are not viable.



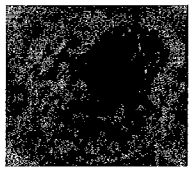
Poorly developing cleavage-stage embryo, unlikely to remain viable.



Implantation: if all has gone well the blastocyst attaches **to and burrows into the uterus on** day 7;
normally at least half of these pregnancies will still fail.

5-6 day embryo (64-128 cells)

= blastocyst



A cavity has formed between the compacted *inner cell mass* (ICM), composed of embryonic stem cells (ES cells) and the *trophectoderm* **(TE), the** trophoblastic (placental) stem cells.

The ability to form a blastocyst **– "blastulation" –** means the embryo is *likely* to be healthy, but at least half are still fatally affected by a genetic condition.

Stem cells are prepared from the inner cell mass.

SYDNEY IVF

RESEARCH PROJECT INVOLVING HUMAN EMBRYONIC STEM CELLS GENERATED FROM EMBRYOS DIAGNOSED BY PGD AS HAVING A GENETIC CONDITION

[LICENSED EMBRYO RESEARCH PROTOCOL 309710]

PARTICIPANT CONSENT FORM

I, _____ and I, _____

Comment [a17]: Paragraph 1

of _____

_____

have read and understood the *Participant Information* explaining the above-named research project and we have discussed the project with _____

We freely choose to take part in this project and understand that we can withdraw our consent without prejudicing our medical treatment or our ongoing professional relationship with medical, nursing or embryology staff at Sydney IVF, should this still be relevant to us. Because the process of deriving embryonic stem cells will destroy our embryos, Sydney IVF will not use our embryos until 2 weeks after we give our consent, in case we decide to withdraw our consent

Comment [a18]: Paragraph 2

We understand that Sydney IVF will keep our taking part in the research study strictly confidential and that we will not be identified. However, we also understand that inspectors appointed by the Embryo Research Licensing Committee of the NHMRC may require access to our records and the outcomes of this research will be reported to the NHMRC Licensing Committee.

Comment [a19]: Paragraph 3

We acknowledge that Sydney IVF may receive a commercial payment from making stem cells available to others. We acknowledge this payment is for the value added from the derivation and testing process and, potentially, the ongoing help Sydney IVF provides another laboratory in further developing or tailoring the cells for that organization's particular research and development program and that we have no claim on any potential payments resulting from the use of our embryos. We understand that we are altruistically donating our embryos for research and development purposes without any restriction or direction regarding the use to which created stem cell lines may be put.

Comment [a20]: Paragraph 4

We have been informed that should we have concerns or complaints about the conduct of the study we can contact the Secretary to the Sydney IVF Ethics Committee Dr Lindsay Gillan (on 8484 6506) or the Chairman of the Committee, Rev'd Dr Ivan Head (on 9550 7444).

Comment [a21]: Paragraph 5

We hereby agree that our embryos produced on [ ] carrying a genetic condition may be used in this research study.

Name: ....

Signature: ....

Date: .....

Name of Witness: .....

Signature of Witness: ..... Date:.....

Document 26

SYDNEY IVF

27 October 2009

Rev'd Canon Dr Ivan Head
Chair, Sydney IVF Ethics Committee
St Paul's College, University of Sydney,
Camperdown, Australia 2050

RE: HREC evaluation and approval of the project: "Derivation of hESC lines from embryos identified through preimplantation genetic diagnosis to be chromosomally or genetically abnormal" (embryo research licence 309710)

To whom it may concern,

On 13 September 2005, the Sydney IVF Ethics Committee convened to discuss the proposed project "Derivation of human embryonic stem cells from embryos identified through preimplantation genetic diagnosis to be chromosomally or genetically abnormal" (licence 309710) and reviewed associated participant information and consent forms. The Committee reviewed the project with reference to the *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (ART guidelines, 2004) and the *National Statement on Ethical Conduct in Human Research*.

Members of the Ethics Committee present for the discussion were:

Rev Dr Ivan Head (Chair)
Dr Edith Weisberg
Mr James Lane
Reverend Peter Kurti
Ms Sandra Dill

Members absent from the discussion were:

Ms Susan Ryan
Mr Rob Ferguson
Rabbi Jacqueline Ninio
Dr Simon Longstaff
Ms Annette McInerney

The five members absent from the discussion received the complete accompanying paperwork and were provided with an opportunity to raise any ethical, compliance or practical concerns regarding the applications and their amendments. No issues with residual implications were raised by them or by any member of the Committee.

As a result of the feedback and discussion, small changes to the patient information were suggested and subsequently incorporated into the documents. The Ethics Committee resolved to approve the study and the associated consent procedure.

Rev. Dr Ivan Head
Chair of Sydney IVF Ethics Committee

Document 28

GENEA
WORLD LEADERS IN FERTILITY

ASSURANCE LETTER

I hereby certify that the derivation of the Genea stem cell lines were conducted under Ethics Committee review and therefore met the requirements detailed in 45 C.F.R. 46, Subpart A.
I also certify that the embryos used for the derivation of these cell lines:

1. were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose; and
2. were donated by individuals who sought reproductive treatment and who gave voluntary written consent for the human embryos to be used for research purposes.

It is Genea policy to allow the donors to withdraw their consent for research until the embryo is actually used. Even after their embryos have been entered into the research protocol, and up until the point a potentially created cell line is distributed outside of Genea, consent can be withdrawn. Embryos may not be intact, but any remnants will then be discarded according to patient's wishes

It is Genea clinical policy that embryos identified as affected by the genetic condition tested for in the PGD department, cannot be used for clinical embryo transfer. Donation of affected embryos to another couple is not desirable or possible. The only options for embryos found to be affected by a genetic condition is to be discarded or to be used (either fresh or after cryopreservation) for research purposes.

The project was performed with a clear separation between clinical and research roles: The treating clinicians were in no way involved in cell line derivation. Researchers were not involved in the clinical care of the patients or the embryo consenting process.

I certify that these statements are true, complete and accurate to the best of my knowledge.

14/12/2011

Dr Tomas Stojanov
CEO and Director of Research

Date

14/12/11

Prof Mark Bowman
Medical Director

Date

Genea Level 2, 321 Kent Street, Sydney, NSW. 2000 Australia
Postal address: GPO Box 4384, Sydney NSW 2001 Genea Limited ABN 82 002 844 448

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f (02) 9233 7519
w genea.com.au

Document 9 29

* these are the first few pages of document 9, which contains all the Australian regulatory documents. They are long so you may wish to view through the database if you need them.

Australian Government
National Health and Medical Research Council
NHMRC

Research Involving Human Embryos Act 2002

Embryo Research Licensing Committee of the NHMRC

LICENCE

This licence is issued under s.21 of the *Research Involving Human Embryos Act 2002*. This licence authorises the use of excess ART embryos specified below, subject to the conditions specified in items 8 and 9 below.

1.	Licence number:	309710
2.	Licence holder:	Sydney IVF Limited
3.	Licence title:	Derivation of human embryonic stem cells from embryos identified through preimplantation genetic diagnosis to be affected by known serious monogenic conditions
4.	Date of issue:	7 May 2007
5.	Licence begins:	7 May 2007
6.	Licence ends:	7 May 2013
7.	Use of excess ART embryos authorised by the licence:	This licence authorises, subject to the Standard Conditions and the Special Conditions, the following uses of excess ART embryos: The derivation of human embryonic stem cell (hESC) lines from cryostored or non-cryostored embryos which have been identified by preimplantation genetic diagnosis (PGD) as being embryos affected by a serious monogenic condition. The hESC lines will be used for the conduct of collaborative research into the molecular biology of serious familial diseases, the development of treatments for the genetic conditions concerned, and the development and testing of drugs.
8.	Standard conditions:	All conditions that are specified in the document *Standard Conditions for Using Excess ART Embryos* as currently published on http://www.nhmrc.gov.au/embryos/monitor/database/index.htm and as amended from time to time.

WORKING TO BUILD A HEALTHY AUSTRALIA
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ABN 88 601 010 284

Australian Government
National Health and Medical Research Council
N H M R C

9.	Special conditions:	All conditions that are specified in the *Special Conditions for Licence No. 309710.*

Note:
The use under this licence of excess ART embryos is subject to the provisions of the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002*. Terms used in this licence which are defined in those Acts carry the same meanings as they do in those Acts.

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Research Involving Human Embryos Act 2002

Embryo Research Licensing Committee of the NHMRC

Special Conditions for Licence No. 309710

Licence number:	309710
Licence holder:	Sydney IVF Limited
Licence title:	Derivation of human embryonic stem cells from embryos identified through preimplantation genetic diagnosis to be affected by known serious monogenic conditions

The conditions that are specified below are the special conditions that apply to this licence. The *Special Conditions* operate **in addition to** conditions set out in s.24 of the *Research Involving Human Embryos Act 2002* (the statutory conditions) and all conditions identified in the *Standard Conditions for Using Excess ART Embryos*. The *Special Conditions* prevail where there is an inconsistency between a special condition and a standard condition.

Conditions relating to embryos

Condition number	*Condition*
9101	The licence holder is authorised to use up to 350 excess ART embryos.
9102	Embryos used for the activities authorised by this licence may be used with or without a period of cryostorage.
9103	This licence is limited to the use of embryos which have been identified by preimplantation genetic diagnosis to have a serious monogenic condition, consistent with the requirements outlined in the NHMRC *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research 2007*.

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ABN 88 601 010 284

9105	Stem cell lines established under this licence count towards the limit stipulated in Condition 9109 when they meet the following criteria: • the embryonic stem cell line possesses a stable human diploid karyotype, expresses immunologically defined markers and genes specific for embryonic stem cells; • results from initial studies indicate that the cell line is pluripotent and capable of self-renewal; • the line has been passaged at least five times in culture, and has been successfully cryopreserved and thawed on two occasions; and • the line has been demonstrated to be free of contamination by adventitious agents.
9106	When eight embryonic stem cell lines have been established in accordance with conditions 9105 and 9109, any remaining cell lines under evaluation may, subject to condition 9402, be used in accordance with the licence.
9107	Excess ART embryos with chromosomal anomalies (eg. monosomies, trisomies and translocations) are not permitted to be used under this licence, with the exception of specified chromosomal anomalies notified to, and authorised by, the Licensing Committee.
9108	The licence holder may not remove from cryostorage for the purpose of conducting the use authorised by the licence a greater number of excess ART embryos than the number specified in condition 9101.
9109	The licence holder is authorised to establish up to eight stem cell lines for each serious monogenic condition.
9110	When eight stem cell lines with an individual serious monogenic condition have been established, no further excess ART embryos identified as having this condition may be used under this licence.

Specified sites

Condition number	*Condition*
9201	The licence holder must conduct the use authorised by the licence at the following site: Sydney IVF Limited 321 Kent St Sydney NSW 2000
9202	The licence holder must hold records (other than patient records) associated with the use authorised by the licence at the following sites: Sydney IVF Limited 321 Kent St Sydney NSW 2000 Filesaver Pty Ltd 2151 Castlereagh Road Penrith NSW 2750

9203 The licence holder must hold patient records associated with the excess ART embryos used in accordance with this licence only at the following sites:

Sydney IVF Limited
321 Kent St
Sydney NSW 2000

Sydney IVF Liverpool
173-175 Bigge St
Liverpool NSW 2170

Sydney IVF Illawarra
3 Urunga Parade
Wollongong NSW 2500

Sydney IVF Newcastle
23 Merewether St
Merewether NSW 2291

Sydney IVF Newcastle
10 Lingard St
Merewether NSW 2291

Sydney IVF Canberra
17B, 2 King Street
Deakin ACT 2600

Sydney IVF Coffs Harbour
Baringa Private Hospital
Mackays Rd
Coffs Harbour NSW 2450

Sydney IVF Lismore
79 Uralba St
Lismore NSW 2480

Sydney IVF Orange
261 March St
Orange NSW 2800

Sydney IVF Tamworth
Tamara Private Hospital
2-6 Dean St
Tamworth NSW 2340

Sydney IVF Launceston
37 Elphin Rd
Launceston TAS 7250

Sydney IVF Northwest
Suite 101, 10 Norbrik Dr
Bella Vista NSW 2153

Filesaver Pty Ltd
2151 Castlereagh Road
Penrith NSW 2750

Persons authorised to use excess ART embryos

Condition number	*Condition*
9301	The Principal Supervisor is responsible for supervision of the activity authorised by the licence. The Principal Supervisor is that person identified at **Attachment A** to this licence.
9302	Only authorised personnel may conduct the activity authorised by this licence. The authorised personnel are the Principal Supervisor and those other persons identified at **Attachment A** to this licence.

Reporting

9402	(a) The licence holder must notify the Licensing Committee in writing within five (5) working days when the combined total of established and potential embryonic stem cell lines with an individual serious monogenic condition equals or exceeds eight. (b) The licence holder must notify the Licensing Committee in writing within five (5) working days when the number of established embryonic stem cell lines per individual serious monogenic condition equals or exceeds eight.
9403	When providing the reports required by Standard Condition 3001, the licence holder must report on the nature of the monogenic condition affecting each embryo used.
9404	When providing the reports required by Standard Condition 3001, the licence holder is required to report on success in establishing embryonic stem cell lines according to the criteria set out in condition 9105.
9405	In addition to the reports required by Standard Condition 3001, the licence holder is required to provide a further written report no later than 6 months following the expiry, revocation or surrender of the licence. This report must use the format specified in the document *Post-expiry report on embryonic stem cell lines derived under a licence issued by the NHMRC Embryo Research Licensing Committee* as published and amended from time to time at the following website: http://www.nhmrc.gov.au/embryos/monitor/application/index.htm

Conditions relating to proper consent

9501	From 14 April2011, only the consent process as described in the documents provided on 9 May 2008, and varied by the documents provided on 30 April 2010, 25 June 2010 and 14 March 2011 and subsequently approved by the Licensing Committee, may be used for obtaining proper consent to use the excess ART embryos identified by PGD as being unsuitable for implantation in the activities permitted by this licence.
9502	When embryos are to be used under this licence without a period of cryostorage, a cooling-off period of at least 12 hours must be observed between the time proper consent is given to use the embryos in the licensed activity and the time of use of those embryos[1].
9503	When embryos are cryostored before use under the licence a cooling-off period of at least 2 weeks must be observed.
9504	The information about the licensed activity ('Participant Information') must be given to prospective embryo donors before proper consent can be obtained. The first time each couple receives the information, it must be provided not less than 2 weeks before the commencement of the ART treatment cycle. For each subsequent treatment cycle a new consent form must be signed before embryos can be donated to the licensed activity[2].
9505	From 21 March 2011, only the Declaration of Excess Embryos form provided on 15 March 2011 and the Participant Information and Consent Form provided on 23 February 2011 and approved by the Licensing Committee may be used for obtaining proper consent to use the excess ART embryos identified by PGD as being unsuitable for implantation in the activities permitted by this licence.

[1] As permitted by s.24(8) of the *Research Involving Human Embryos Act 2002,* this condition modifies the process for obtaining 'proper consent' as prescribed by the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* (as amended in 2007) by reducing the duration of the cooling-off period.

[2] As permitted by s.24(8) of the *Research Involving Human Embryos Act 2002,* this condition modifies the process for obtaining 'proper consent' as prescribed by the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* (as amended in 2007) by requiring provision of information about the licensed activity to prospective embryo donors before embryos are declared to be excess to the reproductive needs of the couples concerned.

Table of Variations

Date of Variation	Conditions Affected	Description of Changes
8 October 2007 (version 2)*	9202, 9203	Addition a site of records storage
8 October 2007 (version 2)	9203	change of Sydney IVF Canberra address
4 December 2007	9302	Removal of two authorised persons from list of authorised persons
28 March 2008 (version 3)	9202, 9203	Removal of site of records storage, addition of new site of records storage
21 April 2008	9302	Removal of authorised person
16 June 2008 (version 4)	Item 7 9102, 9105 New 9501 - 9504	Permission to use non-cryostored embryos
21 August 2008	9302	Addition of authorised person from list of authorised persons
28 August 2008	2001, 2301, 3001, 3101, 3102, 3104, 3201, 3401, 3601, 4001, 4002, 4101, 4102, 4201, 5001	Standard conditions varied to reflect the *Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Act 2006*
20 March 2009 (version 5)	Delete 1001-1004, 2102, 3101-3104, 4001 Add 1101, 3105, 9108 Vary 3001, 4201, 5001, 9301, 9302	Standard Conditions and Special Conditions varied to simplify and clarify requirements
20 March 2009 (version 5)	Expiry Date	Extension of licence to 7 May 2011
2 June 2009 (version 6)	9302	Removal of authorised person from list of authorised persons
27 July 2009 (version 7)	3001, 9406	Standard Conditions and Special Conditions varied to implement revised reporting periods
6 November 2009	9302	Removal of authorised person from list of authorised persons
13 November 2009 (version 8)	9101, 9103, 9104, 9105, 9106, 9402, 9402, 9403 Add 9109, 9110 Delete 9104, 9401, 9406.	Increase to permitted number of embryos; removal of limit to use of embryos diagnosed by PGD as having Huntington's Disease, Cystic Fibrosis or other serious genetic condition; removal of limit to number of stem cell lines permitted to be derived; addition of limit to number of stem cell lines per serious monogenic condition; modification of notification requirement relating to stem cell line limit.

15 April 2010 (version 9)	9203	Addition of site of records storage
15 April 2010 (version 9)	5002, 6001, 6002	Standard Conditions varied to clarify requirements
23 July 2010 (version 10.1)	9501, 9504, 9505	Variation to process for obtaining proper consent
27 January 2011 (version 11)	9501, 9505	Variation to process and documents used for obtaining proper consent
27 January 2011 (version 11)	9302	Removal of authorised person from list of authorised persons
21 March 2011 (version 11.3)	9505	Variation to documents used for obtaining proper consent
14 April 2011 (version 12)	Expiry Date	Extension of licence to 7 May 2013
14 April 2011 (version 12)	9302	Removal of authorised person from list of authorised persons
14 April 2011 (version 12)	9501	Variation to process for obtaining proper consent
20 June 2011 (version 13)	9105	Variation to criteria for established embryonic stem cell lines

* Where a variation resulted in a new version of the licence being issued, the version number is indicated.

From: Julia Schaft
To: HESCREGISTRY (NIH/OD)
Cc: Tomas Stojanov
Subject: RE: New hESC Registry Application Request #2011-ADM-020
Date: Wednesday, February 22, 2012 9:02:02 PM

Dear Dr Gadbois,

Apologies for the delay in getting back to you, unfortunately I was off sick for the past week and unable to give my attention to your question.

In regards to your first question:
Yes, the policy for consent withdrawal that was in place at the time these embryos were donated included informing the patients verbally that withdrawal could occur until the embryo was actually used for stem cell derivation.

There are no written records of what was covered in the phone conversations in each instance. The RCS conveyed general information about the research project to the patients including consent withdrawal options. Patients were always informed according to the company policy described below.

The cooling off period in which embryos could not be used in case the donors wanted to withdraw consent is required by Australian law. Consent forms for the 309710 project (derivation of disease specific stem cells from PGD affected embryos) were developed and reviewed by the Ethics Committee in 2007. The recommendation from the committee in review of the forms included that the *"cooling off period was sufficient opportunity for a change of mind and that 'downstream' ambiguities as to the point at which withdrawal might be possible were considered to be confusing"* (taken from Ethics Committee Meeting Minutes from 6 February 2007). It was for that reason that only withdrawal within the cooling off period was specified in the written form. This position was reviewed at a later stage (2010) and in an effort to uniformise consent procedures for all licences, this led to an update of the written formulation about withdrawal options in the 309710 consent form (see later versions of consent forms e.g. GENEA062).

Please note that embryos consented and used for project 309710 were embryos identified as affected by a genetic condition, were therefore clinically unsuitable and could have never been used for embryo transfer and establishment of a pregnancy, regardless of the consent decision. Genea clinical guidelines stipulate that embryos affected by the conditions tested for, cannot be transferred to the uterus.

In regards to your second question:
The list of our cell lines and their disease status previously provided, only gave reference to single gene mutations detected by preimplantation genetic diagnosis (PGD) analysis. I have expanded the table to also list the karyotype analysis of the cell lines after derivation. You are absolutely correct that GENEA048 has an abnormal karyotype (47XY +5).

Please let me know if there are any further questions.

Kind regards
Julia Schaft

GENEA
WORLD LEADERS IN FERTILITY

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f +61 2 9229 6478
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w genea.com.au
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Please consider the environment before printing

From: HESCREGISTRY (NIH/OD) [mailto:hescregistry@mail.nih.gov]
Sent: Wednesday, 22 February 2012 8:45 AM
To: Julia Schaft
Cc: Tomas Stojanov; HESCREGISTRY (NIH/OD)
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Hello again—I just wanted to confirm that you received the email below with my question.

Also, there is an old Sydney IVF stem cell table we printed out last year that indicated that GENEA048 was 47XY +5. Is that karyotype correct? (The table below indicates that the line is "unaffected.") Please let us know how you would like GENEA048 described on the NIH Registry in the event that the line is approved.

Thanks again,
Ellen Gadbois

From: HESCREGISTRY (NIH/OD)
Sent: Wednesday, February 15, 2012 11:09 AM
To: 'Julia Schaft'
Cc: Tomas Stojanov; HESCREGISTRY (NIH/OD)
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Thanks, Dr. Schaft. Just to make sure we understand: I believe you are saying that the policy for consent withdrawal that was in place at the time these embryos were donated included informing the patients verbally that withdrawal could occur until the embryo was actually used for stem cell derivation. Please confirm if I'm reading this information correctly or if you meant something different.

Sincerely,
Ellen Gadbois

Ellen L. Gadbois, Ph.D.
Office of Science Policy Analysis
Bldg 1 Room 218D
National Institutes of Health
voice: 301-594-2567
fax: 301-402-0280

From: Julia Schaft [mailto:julia.schaft@genea.com.au]
Sent: Monday, February 13, 2012 7:38 PM
To: HESCREGISTRY (NIH/OD)
Cc: Tomas Stojanov; Anna Pirintji
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Dear Dr Gadbois,

The policy for consent withdrawal was in place since 2004 when hESC derivation at Genea commenced. The formal position of the Research Consent Secretary was created in 2005 and staff were trained according to this policy. The training was formalised in 2010 in the form of a written training manual.

Please let me know if you have any additional questions.

Kind regards
Julia

From: HESCREGISTRY (NIH/OD) [mailto:hescregistry@mail.nih.gov]
Sent: Tuesday, 14 February 2012 6:02 AM
To: Julia Schaft; Tomas Stojanov
Cc: HESCREGISTRY (NIH/OD)
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Dear Dr. Schaft and Dr. Stojanov,

Thank you for the response to our questions. I have one follow-up question regarding the withdrawal of consent policy for the embryos from which GENEA017, 041, and 068 were derived (submission 2011-ADM-021). Was the policy you describe in place at the time(s) in 2007 when the embryos were donated? (The RCS training manual is dated November 2010 and your description of the policy in your email response was written in the present tense.)

Please let me know if you have any questions.

Sincerely,
Ellen Gadbois

Ellen L. Gadbois, Ph.D.
Office of Science Policy Analysis
Bldg 1 Room 218D
National Institutes of Health
voice: 301-594-2567
fax: 301-402-0280

From: Julia Schaft [mailto:julia.schaft@genea.com.au]
Sent: Thursday, February 09, 2012 6:32 PM
To: HESCREGISTRY (NIH/OD)
Cc: Tomas Stojanov; Anna Pirintji
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Dear Dr Gadbois,

Thank you for reviewing our submissions and for the opportunity to provide additional information. I endeavour to address all your questions as best I can:

- All hESC submitted by Genea have been derived from blastocyst stage embryos
- No Genea research embryo donor has so far requested translation services. The donors acknowledge on the consent form that they have read and understood the project information given to them. Should translation services be requested, the research department can access Genea translation services offered to our clinical patients.
- The updated assurance letter is attached to this email
- Yes, the GENEA hESC line nomenclature mirrors the earlier SIVF nomenclature (GENEA002 has previously been named SIVF002 etc)
- Please refer to the table below for a description of the disease status of the submitted lines:

hESC line name	Disease Status
GENEA002	unaffected
GENEA017	Affected with Huntington Disease
GENEA018	Affected with Huntington Disease
GENEA024	Affected with Fascio Scapulo Humeral Muscular Dystrophy (FSHD)
GENEA040	Affected with Cystic Fibrosis (CF)

GENEA041	Affected with Cystic Fibrosis (CF)
GENEA046	Affected with Huntington Disease
GENEA048	unaffected
GENEA049	Affected with Fascio Scapulo Humeral Muscular Dystrophy (FSHD)
GENEA050	Affected with Fascio Scapulo Humeral Muscular Dystrophy (FSHD)
GENEA058	Affected with Becker Muscular Dystrophy (FSHD)
GENEA059	Affected with BRCA1
GENEA060	Affected with Van Hippel Lindau Disease
GENEA061	Affected with Van Hippel Lindau Disease
GENEA062	Affected with Charcot Marie Tooth Syndrome
GENEA063	Affected with Charcot Marie Tooth Syndrome
GENEA064	Affected with Charcot Marie Tooth Syndrome
GENEA065	Affected with Infantile Neuroaxonal Dystrophy
GENEA066	Affected with Myotonic Muscular Dystrophy
GENEA067	Affected with Myotonic Muscular Dystrophy
GENEA068	Affected with Wilm's Tumour
GENEA069	Affected with Vitelliform Macular Dystrophy
GENEA070	Affected with Vitelliform Macular Dystrophy
GENEA071	Affected with Incontinentia Pigmenti
GENEA072	Affected with Juvenile Retinoschisis
GENEA073	Affected with Alpha Thalassaemia
GENEA074	Affected with Autosomal Dominant Torsian Dystonia

- The deviation wording in the GENEA48 submission is an oversight. The formulation should be the same for all cell lines "Subject to individual terms and conditions. Please contact us for more information". Genea is currently in the process of reviewing our policy with regards to our cell line distribution. While we were previously providing our cell lines for free under collaborative project agreements, this policy is currently under review and will be finalised within the next months.
- For 2011-ADM-020:
    - At the time the "Sydney IVF Consent For Disposal of Embryos" was in operation (release date 2001), Genea (formerly Sydney IVF) did not offer stem cell derivation from excess ART embryos as an option. Genea received the embryo research licence under which stem cell lines can be derived from excess ART embryos in April 2004. The term "*biochemical tests*" was adjusted in later version of the form to "*scientific studies*" in adaptation to the expanded research focus at Genea.
    - Under Australian law, embryo donation for research has to be a two stage process in which patients have to first declare their embryos as excess to their reproductive requirements before detailed information about research projects can be given to the patients. While patients can declare a general interest in research for their excess ART embryos on the disposal form (later called "*Declaration of Excess Embryos Form*"), specific research consent can only be given in the second stage, after embryos have already been declared as excess. This two stage process has been put in place to protect embryos donors from influencing their decision about the fate of their embryos.
- For 2011-ADM-021: The Genea policy to allow donation withdrawal until the embryo is actually used is communicated to the patient verbally. Genea is employing a Research Consent Secretary (RCS) who is a reference point for embryo donors. While they know a lot about the actual research projects, they are independent from the research team and are able to provide unbiased information to the donors. The RCS is contacting patients to give them opportunity to ask any questions about the consent they are about to be approached with, they can be contacted by the patients at any stage in case of questions and are contacting patients with frozen excess embryos as soon as a suitable research project has been identified for their excess embryos to ask if they would be interested in the project. The topic of consent withdrawal is discussed verbally with the patient. This is reflected in the RCS training manual (excerpt attached). Should the patient

contact Genea with the wish to withdraw consent it is Genea policy to withdraw the donated material from any further involvement in the research:

- If the embryo has not been used yet, it will be returned back into clinical storage (the form in place for these purposes is attached - "*Withdrawal of Declaration of Excess Embryos and Research Consent*").
- If the embryo has already entered the experimental protocol, any cellular material will be disposed off. The embryo cannot be returned to clinical storage due to initiation of the research protocol
- If a hESC line has been derived but has not been distributed outside of Genea, the cell line will be destroyed according to patient's wishes
- Only if the hESC line has already been distributed outside of Genea, consent cannot be withdrawn as Genea has no immediate power over use of the cell line outside the company.

This policy is also reflected in the attached RCS training manual excerpt. Please note that the Genea process for consent and its withdrawal has been reviewed by the Australian National Health and Medical Research Council (NHMRC) on numerous occasions. It is in full compliance with Australian regulatory requirements and fully approved by our Human Research Ethics Committee.

- The draft submission of SIVF017 can now be deleted from the NIH hESC submission system, it has indeed been superseded with the recent submission of GENEA017 etc. Thank you.

I hope I have been able to address all your questions to your satisfaction. Please don't hesitate to contact me again for any further assistance I can provide.

Kind regards
Julia Schaft

GENEA
WORLD LEADERS IN FERTILITY

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w genea.com.au
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Fr70om: HESCREGISTRY (NIH/OD) [mailto:hescregistry@mail.nih.gov]
Sent71: Friday, 27 January 2012 6:16 AM
To: To72mas Stojanov; Julia Schaft
Cc: HESC7REGISTRY (NIH/OD)
Subject: RE: New hESC Registry Application Request #2011-ADM-020

Dear Dr. Stojanov and Dr. Schaft,

Thank you for your recent submissions to NIH. We have begun the administrative review process on submissions 2011-ADM-020 (for lines GENEA 002 and 048) and 2011-ADM-021 (for lines GENEA 017, 041, and 068). The administrative review group has several questions regarding these submissions, several of which also pertain to your other submissions which we have not yet begun to review.

For all submissions:

- For all hESC lines submitted, can you please confirm that they are derived from blastocyst-stage embryos? Please be aware that the only hESC lines eligible for consideration under the NIH Guidelines for Human Stem Cell Research are from blastocyst-stage embryos.
- Please indicate whether any embryo donors required translation services; if yes, please describe that process.
- Please use the current language template for the assurances from Dr. Stojanov. We changed that language a few months ago to address translation issues that have arisen. You can find the current language at the link from "A sample letter (MS Word - 44 KB) is provided for this purpose" at http://hescregapp.od.nih.gov/NIH_Form_2890_Login.htm
- Does the GENEA line nomenclature mirror the earlier SIVF nomenclature (e.g. is GENEA002 the same as SIVF002)?
- Please indicate whether any of the lines have disease-specific or other genetic mutations. This does not affect the decision of whether the lines are eligible for use in NIH-funded research under the NIH Guidelines for Human Stem Cell Research, but is helpful information for NIH grantees if the lines are approved and listed on the NIH Registry.
- Can you provide more detail regarding the "Provider Restrictions" that list: "Subject to individual terms and conditions. Please contact us for more information"? We note that GENEA048 instead states "Subject to individual Material Transfer Agreement between recipient and GENEA." Please be aware that these restrictions do not affect the decision of whether the lines are eligible for use in NIH-funded research under the NIH Guidelines for Human Stem Cell Research, but since the two restrictions are different, it may be confusing to NIH grantees if these lines are approved and listed on the NIH Registry.

For 2011-ADM-020:

- Please explain why the original "Sydney IVF Consent For Disposal of Embryos" (signed 26-1-04) does not include research involving the derivation of stem cells as a possible option.

For 2011-ADM-021:

- Please explain if the donors were informed of the full GENEA policy regarding withdrawal of consent. We note the language in the Participant Information and Consent form regarding the two week period during which donors may withdraw consent, but also note that you state that is it GENEA policy to allow donors to withdraw their consent for research until the embryo is actually used.

For your draft submission on line SIV017: should we delete this from the system? We are guessing that submission 2011-ADM-021 (for lines GENEA 017, 041, and 068) actually covers the SIV017 line.

Please let me know if you have any questions regarding this inquiry. You can send any additional documentation by email to us at this email box and we will update your submissions.

Sincerely,
Ellen Gadbois

Ellen L. Gadbois, Ph.D.
Office of Science Policy Analysis
Bldg 1 Room 218D
National Institutes of Health
voice: 301-594-2567
fax: 301-402-0280

From: HESCREGISTRY (NIH/OD)
Sent: Sunday, December 18, 2011 8:41 PM
To: tomas.stojanov@genea.com.au; julia.schaft@genea.com.au
Subject: New hESC Registry Application Request #2011-ADM-020

To: Tomas Stojanov (Signing Official)
Julia Schaft (Submitter)

This is to confirm that the hESC Registry Application request, as detailed below, has just been submitted and is pending NIH Administrative review. You can expect to hear back from us about the status of your application soon.

While pending review, the name of the stem cell line (Question 6) will appear on the public NIH Human Embryonic Stem Cell Registry for Submitted hESC Lines Pending Review.

After review, your organization name and name of the stem cell line(s) will be posted on the Web page either as "Lines Eligible for NIH Funding" or "Lines not Approved."

If the cell line is approved for inclusion on the NIH Registry, information entered into Questions 6-9 will be posted on the NIH Human Embryonic Stem Cell Registry for hESC Lines Eligible for NIH Funding.

If you have any questions about the hESC Registry Application process, please contact us.

Thank you,

hESC Registry Help Desk
hescregistry@mail.nih.gov

hESC Registry Request Information
for NIH Administrative Review

Request #:	**2011-ADM-020** (Previously: 2011-DRAFT-015)
Status:	**Pending** (12/18/2011)
Administrative Information:	
1. Signing Official (SO):	**A.** Name: Tomas Stojanov **B.** Phone: +61-2-84846505 **C.** Email: tomas.stojanov@genea.com.au
2. Submitter of Request:	**A.** Name: Julia Schaft **B.** Phone: +61-2-92296449 **C.** Email: julia.schaft@genea.com.au
3. Organization Name and DUNS	GENEA DUNS: 750354490
4. Organization Address:	Level 2, 321 Kent Street, Sydney NSW 2000 AUSTRALIA
5. NIH Grant or Application Number(s):	
Stem Cell Line #1 Information:	
6. Name of Stem Cell Line:	GENEA002
7. Cell Line Available:	Yes
8. Provider Restrictions (if any) on Use of Stem Cell Line:	Subject to individual terms and conditions. Please contact us for more information
9. Provider of Stem Cell Line:	**A.** Name: GENEA **B.** Phone: **C.** Email: julia.schaft@genea.com.au **D.** URL:
10. Embryo Donation:	**A.** In United States: No **B.** Year(s) of Donation: 2005
Stem Cell Line #2 Information:	
6. Name of Stem Cell Line:	GENEA048
7. Cell Line Available:	Yes
8. Provider Restrictions (if any) on Use	Subject to individual Material Transfer Agreement between

of Stem Cell Line:	recipient and GENEA
9. Provider of Stem Cell Line:	**A.** Name: GENEA **B.** Phone: **C.** Email: **D.** URL:
10. Embryo Donation:	**A.** In United States: No **B.** Year(s) of Donation: 2005

Supporting Information (Document Attachments):

Document 1:	Document 1 (PDF - 12/15/2011) Description: Assurance Letter and Business Name Registration Supported Elements: Other
Document 2:	Document 2 (PDF - 12/15/2011) Description: Summary of Supporting Information Supported Elements: Other
Document 3:	Document 3 (PDF - 12/15/2011) Description: Overview of the Consenting Process Supported Elements: Other
Document 4:	Document 4 (PDF - 12/15/2011) Description: Mapping of the Elements Supported Elements: Other
Document 5:	Document 5 (PDF - 12/15/2011) Description: ISO consent forms Supported Elements: 1,2,3,4,5,7,8,9,10,11,12,13,14,15
Document 6:	Document 6 (PDF - 12/15/2011) Description: HREC Approval Supported Elements: Other
Document 7:	Document 7 (PDF - 12/15/2011) Description: Publications Supported Elements: Other
Document 8:	Document 8 (PDF - 12/15/2011) Description: Assurance Letter Supported Elements: 1,2,5,6,8
Document 9:	Document 9 (PDF - 12/15/2011) Description: Assurance Letter Finance Supported Elements: 3,4
Document 10:	Document 10 (PDF - 12/15/2011) Description: Regulatory Documents Supported Elements: 1,2,3,4,5,6,7,8,9,10,11,14

Comments:

12. Comments:	Please note that our company name has changed from Sydney IVF to Genea in 2011. Some references in our supporting documents are to the old company name.

Assurance, Certification, Authority:

Assurance Checked:	No
Certification Checked:	No
Authority Checked:	No

Login Information: Commons\T.Stojanov
Date/Time: 12/18/2011 at 08:40:44 PM

Attached to 2/9/2012 email

Genea Training Manual

Research Consent Secretary

309701
309702A
309702B
309703
309710
309712
309713
309714
Clinical investigation embryonic outgrowths

November 2010

Contents

Clinical Investigation embryos (I-embryos) –outgrowths
Background
Process

Information letters

Process embryos that have been declared as excess
Background
Allocating excess ART embryos to research (City)
Allocating excess ART embryos to research (Satellite Clinics)

Consenting embryos to 309701, 309702A+B and 309703

Consenting embryos to 309710

Reference point for patients with questions about research

SCNT reminder calls

Donor Update Letter

Licensed Research Projects at Genea

Embryo/Egg donation in general

Do's and Don't's

Embryo/egg donation in general

- Consent to donate excess ART embryos to research is completely voluntary and free from coercion. The decision whether to participate in research or whether to withdraw consent will have no effect on the patient care or clinical treatment.
- There is a clear separation between the clinical care of the patient and research requirements.
- There is no payment or inducements for the donation of embryos or gametes.
- While we intend our research projects and subsequent research and development studies to advance medical knowledge (and to assist in the development of new treatment for diseases), it would normally be unlikely to benefit the patient in the immediate future.
- Counselling services are available to the patients at any time
- Donor privacy will be protected. Only the scientists directly responsible for the laboratory procedures involving cells from the embryos will have access to potentially linking information between the cells and the patient. It is unlikely but theoretically possible to identify the donor through DNA matching even if their genome is only partially represented in the study. Inspectors appointed by the Embryo Research Licensing Committee of the National Health and Medical Research Council (NHMRC) can require access to patient records for auditing purposes to ensure Genea meets the requirements of the legislation. A report of our and others' work may be submitted for publication, but individual participants will not be identifiable in such a report.
- Consent is specific; we will only be able to use the embryos for the specific project detailed in the signed consent form.
- Not all embryos consented to a specific project may necessarily be used – it depends on the requirements and logistics of the research. In case consented embryos are not used for our research by the time this project expires (e.g. because we have consent to use more embryos than the research licence allows us to use) they might become eligible for a different project. Unless asked not to, we will then contact the patient again with other research options at Genea or the option to discard remaining embryos after expiry of the project/licence. It is the patient's responsibility to keep contact information up to date. We will take any reasonable means to get in touch with the patient, but should we not be able to re-contact them, the default option for remaining frozen consented embryos after expiry of the project is to leave them to succumb and be discarded.
- Patients who donate embryos for research purposes will receive regular updates on the progress and/or outcome of the specific project(s) they request not to.

- In case of complaints the patient can contact the Secretary of the Ethics Committee.
- Consents have to be returned within 6 months of receiving the consent documents. If signed consents are not returned within this time, embryos re-enter the paid storage agreement and an invoice for storage will be sent to the patient.
- There are specific requirements for the donation of embryos if one partner has died. Embryos cannot be donated unless the partner who has died has not previously given specific consent. Organ donor registration does not constitute consent to the donation of embryos.
- Consent can be withdrawn within a two week waiting period after signing the consent form. In other words, embryos will not be used for at least two weeks, which gives the patients this time to reconsider their decision. Ultimately consent can be withdrawn until embryo has been actually entered into the study.

Additional information specific to 309703 (stem cell derivation)

- The patient will be asked for further consent before stem cells derived from their embryos are allowed to be used for further research and/or to leave Genea (Consent for Stage 2).
- After second stage consent cell lines may be distributed worldwide and may be studied for many years. Cell lines may be used for ethically approved stem cell research and development purposes without any restriction or direction regarding the use to which they may be put or regarding who may be the recipient of transplants of the cells derived.
- Any other restrictions the patient would like to put on the use of a potentially created stem cell line have to be specified in the comments section on the consent form.
- Genea may receive a commercial profit from making the cell lines available to others. This payment is for the "intellectual property" arising from the development and testing processes as well as for ongoing help Genea provides other laboratories in further developing or tailoring the cells for that organization's particular research and development program.
- Consent can be withdrawn within a two week waiting period after signing the consent form. In other words, embryos will not be used for at least two weeks, which gives the patients this time to reconsider their decision. Even after embryos have been entered into the study, the patient can still choose to withdraw consent at any time until the cell lines leave Genea (after second stage consent for distribution). However if embryos have already entered the experimental protocol they may no longer be intact.

Do's and Don'ts

Always act professionally, knowledgeable and confident. The patient has to be assured that his embryos are in responsible and professional hands!

Use simple and lay language to communicate with the patient. Refrain from the use of technical or scientific terms.

Retain a neutral position. You are acting as a link between the patient's interests and the research team. You should not be considered as taking any position in the conversations.

Always treat the patient with respect, no matter how often the matter has already been discussed, or how silly the question might seem.

Never apply any form of coercion. Embryo and gamete donation is completely voluntary and entirely independent of research requirements.

In case you cannot answer a question with confidence, let the patient know and consult the research team or other relevant sources before getting back to the patient.

Before contacting a patient please familiarise yourself with all the relevant personal patient details (family, pregnancy, partner etc) by consulting Genea databases.

Never mention that you are calling from "Genea" unless you are certain that you are speaking with the correct person.

Attached to 53
2/9/2012 email

Patient name: _____

Date of birth: _____

MRN (if known): _____

GENEA
WORLD LEADERS IN FERTILITY

Withdrawal of declaration of excess embryos and research consent

I,(full name):_____

Date of birth:_____

and (full name) _____

Date of birth:_____

Of (address):_____

_____

We declare that the embryos produced from our eggs and sperm on Genea to insert date and in stored in the research cryostorage facility at Genea are now no longer excess to our reproductive needs and we withdraw our consent for research if this has been given.

We request that Genea accept our frozen embryos from the Genea research cryostorage facility into the general Genea cryostorage facility for possible future use.

We understand that:

1. We will be charged a fee for storing our embryos.
2. the embryos might not survive the freezing and thawing process
3. the embryos might not produce a pregnancy after thawing and transfer
4. Genea reserves the right to discontinue the service of storing reproductive tissues and that in this circumstance Genea will attempt to advise us on alternative locations at which such storage might be continued. We also understand that there might be additional costs attached to such cryostorage.
5. Genea may discontinue storage without further warning in circumstances including:
   - One year passes during which we fail to request storage to be continued after an enquiry to this effect is posted to our last address given by us to Genea.
   - One year passes after notification to us at the last address known to Genea that continued storage is for any reason not possible, and we have not completed alternative arrangements for continued storage.
   - One year passes during which there has been no payment of any fees payable for continued cryostorage.
   - It becomes required by law.

Genea strongly advises that you amend your Will to indicate your intentions for use or disposal of your embryos in the event of your death. Particularly, you should indicate your agreement (or not) that your partner has future access to this tissue in your absence.

Please note there may be legislation, regulations and/or policies that limit the use of this tissue after the death of the signatory

_____
Signature

_____
Full Name of Witness (print)

_____
Signature of Witness

Date:_____

_____
Signature of Partner

_____
Full Name of Witness (print)

_____
Signature of Witness

Date:_____

GENEA
STEM CELLS

GENEA
WORLD LEADERS IN FERTILITY

Date: 27/04/2012

GENEA
Level 2, 321 Kent Street
SYDNEY 2000
AUSTRALIA

NIH Stem Cell Registry:

I hereby certify that the statements in the Request for Genea Human Embryonic Stem Cell Lines GENEA017, 018, 024, 040, 041, 060, 061, 064 and 068 (submissions 2011-ADM-21 and 2011-ADM-22) to be Approved for Use in NIH Funded Research (NIH Form 2890), submitted by Dr Julia Schaft, and below, are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties (U.S. Code, Title 18, Section1001). I also hereby confirm that any materials translated into English were accurately translated by an individual independent of my institution, who is fluent in English and the original language of the translated documents.

I further confirm that that I have the authority and/or rights pertaining to the human embryonic stem cell lines identified in item 6 of the form to make this request for NIH review and determination of eligibility for use in NIH funded research (e.g., I am the owner, deriver or licensee or have written permission of the same to submit). Any and all restrictions on the use of the stem cell lines are clearly and completely identified in item 8 of the form.

Assurance Statement:

__X___ Assurance in accord with Section II(B) of the NIH Guidelines:

I hereby assure that the embryo from which the cell line(s) identified in item 6 of the form was derived was donated prior to July 7, 2009, and the embryo: 1) was created using in vitro fertilization for reproductive purposes and was no longer needed for this purpose; and 2) was donated by individuals who sought reproductive treatment ("donor(s)") who gave voluntary written consent for the human embryo to be used for research purposes

I acknowledge that I have read, understood, and agreed to the information provided on the form, including the Instructions for completing the form, and the Certification, Authority and Assurance provided above.

Dr Tomas Stojanov
CEO and Director of Research