COVER PAGE

Study Title: Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

NCT02925390

Responsible Party: Patrick Yeung, MD

Documents: Study Protocol and Statistical Analysis Plan

Date of Study Protocol document: Submission date 12.10.2019 (printed 8.10.2020)

Protocol Title:	Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage
Protocol Status:	APPROVED
Date Submitted:	12/10/2019
Approval Period:	01/09/2020-01/19/2021
Important Note:	**This Print View may not reflect all comments and contingencies for approval. Please check the comments section of the online protocol. Questions that appear to not have been answered may not have been required for this submission. Please see the system application for more details.**

* * * Continuing Review * * *

Continuing Review Request

WHAT TO UPLOAD WITH YOUR CONTINUING REVIEW APPLICATION

For studies where research activities are limited to data analysis, upload subject safety information and publications (e.g., manuscripts, abstracts) since the last IRB approval, if applicable.

NOTE: if activities are limited to data analysis of de-identified/anonymous data (data that can no longer be linked to subject identifiers directly or through use of a code with master list kept), the study can likely be closed via the Final Report Form. See the SLU IRB Guidance for Closure of Human Subjects Research Studies.

For all other studies, upload:

- Subject safety information including the most current Serious Adverse Event (SAE) cumulative table and data safety monitoring reports since the last IRB approval, if applicable.
- Any publications (e.g., manuscripts, abstracts) since the last IRB approval.

Any changes, updated and/or new study materials should be uploaded and questions 19 - 24 of this form should be completed.

1. **Please indicate the status of the study:**

   a) **The study has not started but will become active.**
   Please explain why the study has not started.

   b) X **The study is ACTIVE (please check the appropriate box below):**
   Study is open to accrual.
   Study is on hold or halted.
   Please explain what needs to occur before accrual can resume.

   X **Study is permanently closed to accrual.**

   i. Y Have all subjects completed all research related

activities/interventions?

ii. N Will the research only remain active for long-term follow-up of subjects?

iii. Y Are remaining research activities limited to data analysis only? (See instructions above).

iv. N For studies that are closed to subject accrual, do any subjects need to be re-consented (to inform them about changes to study procedures, study risks, study personnel, etc.)?

For IRB office use: * may qualify for expedited review

c) **The study has expired and needs to be re-initiated.**
Explain any research activities occurring during lapse in IRB approval.

2. **Date the study was initially approved by the IRB:** 01/20/2016

3. **Approval date of previous continuing review:** 01/08/2019

4. **Total number of participants/records/specimens you are approved to enroll.** 600 participants (300 women and 300 partners)

5. **Total number of subjects that have given consent (verbal or written) to date.** 72 (45 women + 27 male partners)

6. **Total number of subjects that failed screening (if not applicable, state N/A).** 0

7. **Total number of participants accrued since the beginning of the project.** 72 (45 women + 27 male partners)

8. **For multi-center studies, number of subjects approved for accrual study-wide (SLU site plus all other sites).** N/A

9. **For multi-center studies, number of subjects enrolled study-wide (SLU site plus other sites).** N/A

10. **Number of withdrawals from the research and explanation/reasons for withdrawals.**

None

11. Description and number of:

a) Reportable Protocol Deviations/Violations since the last approval date:

None

b) Unanticipated Problems (UPs) since the last approval date:

None

c) Serious Adverse Events (SAEs) since the last approval date:Note: Information here should be consistent with the cumulative table, which should also be attached in section #16.

None

12. Have there been any complaints about the research during the last year? N

If yes, please describe.

13. Briefly describe the progress of the study to date. Provide a status of participants in study, for example, where is the most recently accrued participant in terms of timeline in the study? If participants are in long-term follow-up, explain what this consists of in terms of data collection and/or intervention. Provide any new information in regard to risks. Summarize or attach publications or presentations.

There has been no subject enrollment since last continuing review approval 1/19/2019. Follow up completed. Data analysis and manuscript being done.

14. Is there a Data Safety Monitoring (DSM) plan for this study?

Y No

Yes, a copy of the DSM report(s) for the last approval period is in the Attachments section.

Yes, but a copy of the DSM reports(s) for the last approval period is not attached. Please explain below.

15. FDA Regulated Studies

Is this a Food and Drug Administration (FDA) Regulated Study, (i.e., involves drugs, devices, biologics)? If yes, please answer the following questions: N

a) Have there been any changes in the FDA status of any drug or device used in the study?

If yes, please explain:

b) Have any of the investigational drugs or devices used in this study received FDA approval?
If yes, please explain:

c) Have any new alternative drugs or devices been approved for treatment of the study condition that may affect subjects willingness to participate?
If yes, please explain:

Have current subjects been notified? Please explain:

d) Has there been a change in the standard care that may be considered as an alternative to the investigational drug or device or that would affect the original study design?
If yes, please explain:

Have current subjects been notified? Please explain:

e) Is there any new information that might affect the risk/benefit ratio and the willingness of current study subjects to participate or to continue to participate in the research?
If yes, please explain:

Have current subjects been notified? Please explain:

f) Does the study include an investigator's brochure (IB)?
If yes, what is the current version date?

(If study has multiple IBs, attach current versions in Attachments section (#16))

16. Provide a summary of any recent findings, literature, or other relevant information (especially pertaining to risks), if applicable.

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Oral presentation at international conference of American Association of Gynecologic Laparoscopists (AAGL) 2019 in Vancouver Canada. Findings, no difference in abnormal pathology of appendix.

17. **Have there been any significant amendments or revisions to the protocol during the past approval period? (Significant amendments include changes in study design or risk level including those that resulted in a change in consent).** N

If yes, please briefly summarize the changes:

18. N/A The consent materials attached to this eIRB application (including consent documents, assent documents, recruitment statements or other materials used to obtain consent) are the versions being used in the conduct of this study and all enrolled subjects have signed consent forms on file, if required. (If the requirement to obtain consent was waived or if no participants have enrolled since last continuing review, check N/A).

NOTE: The IRB routinely monitors consent document usage and may request copies of redacted participant consent forms.

19. **Are any changes (amendments) requested with this Continuing Review?**

Yes, please complete the remainder of this form.

Y **No, form is complete. Please submit.**

20. **Summarize the proposed changes to the protocol in lay terms, including the type of change AND what the change involves.**

If this is a change in PI a new Department Chair review is required. Please upload the signed document in the Attachments section.

21. **Provide justification/explanation for the proposed changes.**

22. **Will currently accrued subjects need to be notified of changes?**

If no, please justify why not.

If yes, please explain how AND when notification or re-consenting will occur.

23. **Does the SLU IRB Protocol need to be modified?**

24. **Are consent documents modified?**

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Proceed to the appropriate section(s) of the protocol and make your changes. Also make necessary changes in the Consent Form(s), Assent Form(s), Recruitment Statement, Questionnaire, or other attachments, as applicable. Upload any revised IRB materials. Please provide the entire revised document (not just revised pages). Use track changes or highlight (in yellow) changes to documents being revised. Please upload a tracked/highlighted copy of each revised document to be stamped upon IRB approval. NOTE: Upload a clean copy (changes or highlights removed) of documents in file formats other than Microsoft Word (i.e., the IRB will remove the tracked changes/highlights on uploaded Word documents).

NOTE: Protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects.

Sponsored Studies: Remember to update the Sponsor's Protocol version number and date in the Funding section of the protocol (this information will appear on the approval letter).

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* * * Personnel Information * * *

Study Personnel Roles:
-Principal Investigator: accepts responsibility for study, must sign obligations, can edit protocol and submit to IRB
-Administrative Contact: additional study contact, may or may not also be member of research team, can edit/prepare protocol and submit to IRB
-Key Personnel (Research Team): SLU member of research team, can view protocol (not edit)
-Non-SLU Collaborator: member of research team from another institution or organization outside of SLU, has no access to system, must be provided with PDF of protocol. NOTE: SLUH/SSM employees who collaborate regularly may obtain a guest SLU account if access to system is needed.
-Department Chair: Official Department Chair, may or may not also be a member of research team, can view the protocol (not edit). NOTE: a proxy may be listed if the Chair is the PI.

IMPORTANT NOTE: Human Subjects Protection Training is mandatory for all research team personnel.

Principal Investigator (PI) Mandatory

PI must be SLU affiliate.

Name of Principal Investigator (Faculty, Staff or Student)	Degree (MD/PhD)	Title
Yeung, Patrick	MD	Associate Professor
Email	**Phone**	**Fax**
pyeung1@slu.edu	(314) 781-8605	

Department Name
Ob/Gyn-Minimally Invasive Gyn

Human Subjects Training Completed? Y
WARNING: Proof of training must show below or the application will be returned. If your training information isn't showing, upload a copy in the Attachments section.

Research Experience ***?HELP?***

Has over 8 years of research experience including design, implementing, data collection and analysis.

Research Team Member Duties Picklist

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1.	X	Recruitment	2.	X	Obtains consent
3.	X	Determine Subject Eligibility for Accrual	4a.		Subject Physical Examinations
4b.		Follow-up Visits including physical assessments	5.		Perform study procedures or Specimen Collection
6a.		Administer and/or Dispense Study Drugs, Biologics or Devices (must be licensed)	6b.		Receive, Store, Manipulate or Account for Study Drugs, Biologics or Devices
7.		Subject Randomization or Registry	8.	X	Collection of Subject Data
9.	X	Report Data (CRFs, e-CRFs, Spreadsheets)	10.		Data Analysis
11a.		Review Adverse Events	11b.		Treat and Classify Adverse Events
12.		Other (Please insert explanation below.)			

UserID	CourseCompletionDate	Course
pyeung1	11-08-2012	Good Clinical Practice (GCP)
pyeung1	08-11-2017	Good Clinical Practice (GCP) Refresher
pyeung1	07-22-2009	CITI/University of Miami Training
pyeung1	03-11-2013	CITI Biomedical Research Refresher Training

Administrative Contact

Name of Administrative Contact	Degree	Title
Mathews, Katherine	MD	Associate Professor
Jamalabadi-Majidi, Shohreh	MPH, DMD	Research Coordinator

Key Personnel (Research Team)

Name of Key Personnel (Research Team)	Degree	Title	Department Name
Treiman, Sierra	Medical Student	Student	Ob/Gyn/Women's Health
Voltz, John	MD	Housestaff Resident	Ob/Gyn/Women's Health

Department Chair Mandatory

The official Department Chair should be listed here. If the Department Chair is the PI, a proxy may be listed.

Name of Department Chair Degree Title

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McLennan, Mary | MD | Professor

Email | **Phone** | **Fax**

mclennan@slu.edu | (314) 781-1031

Department Name

Ob/Gyn-Administration

Is this individual also a member of the research team? N

Human Subjects Training Completed?
WARNING: Proof of training must show below or the application will be returned. If your training information isn't showing, upload a copy in the Attachments section.

Research Experience *?HELP?*

Research Team Member Duties Picklist

1.	Recruitment	2.	Obtains consent
3.	Determine Subject Eligibility for Accrual	4a.	Subject Physical Examinations
4b.	Follow-up Visits including physical assessments	5.	Perform study procedures or Specimen Collection
6a.	Administer and/or Dispense Study Drugs, Biologics or Devices (must be licensed)	6b.	Receive, Store, Manipulate or Account for Study Drugs, Biologics or Devices
7.	Subject Randomization or Registry	8.	Collection of Subject Data
9.	Report Data (CRFs, e-CRFs, Spreadsheets)	10.	Data Analysis
11a.	Review Adverse Events	11b.	Treat and Classify Adverse Events
12.	Other (Please insert explanation below.)		

UserID	CourseCompletionDate	Course
mclennan	01-26-2018	Good Clinical Practice (GCP)
mclennan	01-19-2018	CITI Biomedical Research Refresher Training
mclennan	01-11-2001	Protecting Study Volunteers in Research

Research Team Roles

Name(s), Degree	Department	Experience	Duties
Yeung, Patrick, MD	Ob/Gyn-Minimally Invasive Gyn	Has over 8 years of research experience including design, implementing, data collection and analysis.	Recruitment, Obtains consent, Determine Subject Eligibility for Accrual, Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets)
Treiman, Sierra, Medical Student	Ob/Gyn/Women's Health	limited research experience, but will be mentored by the experienced staff	Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis

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Voltz, John, MD	Ob/Gyn/Women's Health	conducted chart reviews on a several hundred patients for a study on cesarean sections. Limited research experience mentored by experienced research team.	Collection of Subject Data, Report Data (CRFs, e-CRFs, Spreadsheets), Data Analysis

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* * * Subject Population * * *

Subject Population(s) Checklist

Select All That Apply :

X Adults
Cognitively Impaired Subjects
Employees (specifically targeted)
Fetuses
Minors (under 18)
Neonates
Non English Speaking Subjects
Pregnant Women
Prisoners
Students (specifically targeted)
Terminally Ill Subjects
Wards of the State
Other (any population that is not specified above)

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* * * Study Location * * *

Study Location(s) Checklist

Indicate where the study will be conducted. Select all that apply:

Saint Louis University, Medical Center Campus
Saint Louis University, Frost Campus
Saint Louis University, Madrid Campus
X Saint Louis University, SLUCare Practice Locations
SSM STL (DePaul Hospital, St. Mary's Health Center, St. Joseph (St. Charles, Wentzville, Lake Saint Louis), St. Clare)
Cardinal Glennon Children's Medical Center
Saint Louis University Hospital (SSM Health- SLU Hospital)
SLU-SSM Cancer Center Research Alliance Sites
Other (In the box below, list any off-campus institutions or locations and describe the activities being conducted there. Please provide letters of cooperation and/or IRB approvals from each location to document support/approval of the study. You may provide such documentation as it becomes available, but

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you may not begin work at those sites until documentation of support is provided to the IRB.) Please refer to the Guidance for involving non-SLU institutions in human subject research.

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* * * General Checklist * * *

General Checklist

Select All That Apply :

- Collection of Specimens
- X Data collection via e-mail or the Internet
- Deception/Incomplete Disclosure
- Dietary Supplements, Vitamins, and Other Food Agents
- FDA Approved Device
- FDA approved drugs, reagents, other chemicals administered to subjects (even if they are not being studied), or biologic products
- Genetic Testing
- HIV Testing
- Human blood, cells, tissues, or body fluids
- International Research or Research on International Populations
- Investigational drugs, reagents, chemicals, or biologic products
- Investigational Device
- X Investigator Initiated Study *?HELP?*
- X Medical Records
- Photography, Video, or Voice-Recording Subjects
- X Questionnaires and/or tests
- Radioisotopes/radiation-producing machines, even if standard of care
- rDNA/Gene Transfer Therapy
- Registry(ies)
- Specimens to be stored for future research projects (must be in consent form)
- Study of existing data or specimens
- X University Indemnified Study (SLU is responsible for liability coverage) *?HELP?*
- Other (clarify in text box to the right)

Single Use. Provide a brief summary and justification for the Single Use Therapy. Note: This application will refer to research. For Single Use applications it is understood that 'research' will mean 'therapy'.

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* * * Funding * * *

Funding Checklist

Protocol Title: Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

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X NONE

NOTE: Applicable grant application, contract or subcontract, investigator's brochure, and sponsor's protocol (for all industry sponsored clinical trials) must be attached. You will be prompted for these in section #16 (Attachments).

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* * * Expedited Paragraphs * * *

To request an Expedited Review, check the appropriate category(ies) below. Provide justification for your request for Expedited Review.

To qualify for expedited review, research activities must (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories below.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

a) Research on drugs for which an investigational new drug application (21 CFR Part 31, 32) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

b) Research on medical devices for which

(i) An investigational device exemption application (21 CFR Part 812) is not required; or

(ii) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

From other adults and children, considering the age, weight, and health of the subjects, the

collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

Children are "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."

3. Prospective collection of biological specimens for research purposes by non-invasive means.

EXAMPLES: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra-and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

EXAMPLES: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subjects' privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiology; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight and health of the individual.

X 5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

This is a prospective cohort observational study. Couples presenting for possible treatment with natural procreative technology, or NPT will be recruited for participation in the study. Observation of the characteristics of the couples, the nature of the NPT treatments, and the outcomes including live births will be followed for up to 3 years for each couple entering the study. Data will be collected from medical records from consent to 3 years of treatment or follow up. See data collection sheet in section 16.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

X 7. Research on individual or group characteristics or behavior (including, but not limited to, research on

perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

This is a prospective cohort observational study. Couples presenting for possible treatment with natural procreative technology, or NPT will be recruited for participation in the study. Observation of the characteristics of the couples, the nature of the NPT treatments, and the outcomes including live births will be followed for up to 3 years for each couple entering the study. Participants will completed surveys at entry, childbirth, yearly time points and if they exit the study before completing the 3 year follow up.

8. [FOR IRB use only]. Continuing review of research previously approved by a convened IRB only when condition (a), (b), or (c) is met.

   a) Previously approved research where
      (i) The research is permanently closed to the enrollment of new subjects;
      (ii) All subjects have completed all research-related interventions; and
      (iii) The research remains active only for the long term follow-up of subjects.

   b) Previously approved research where no subjects have been enrolled and no additional risks have been identified.

   c) Previously approved research where the remaining research activities are limited to data analysis.

9. [FOR IRB use only]. Continuing review or research not conducted under an investigational new drug application or investigational drug exemption where expedited categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

* * * Background, Purpose, Study Procedures * * *

Title

Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

Complete Sections 1 - 16. In sections that allow reference to sponsor protocol or grant, clearly state section and page numbers. Any information that is different or specific to the local site should be in the SLU application. Specify N/A as appropriate.

1. Background

Page numbers from a sponsor's protocol/grant may be referenced in 1a and 1b.

a) **Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of the study, if applicable. Investigator initiated studies must cite references in the response provided or attach a bibliography. *?HELP?***

cite references in the response provided or attach a bibliography. *?HELP?*

Infertility is a common problem. While most of current clinical research of infertility focuses on in vitro fertilization and related techniques of assisted reproductive technology (ART), some couples do not wish to use in vitro fertilization, or cannot afford it. Natural procreative technology (NPT) is a standardized approach to the treatment of infertility that does not involve ART. NPT incorporates standard infertility treatments (such as clomiphene or progesterone) within a set of standardized application protocols. The goal of NPT is to identify abnormalities of the woman's reproductive cycle (menstrual cycle), and where possible, correct them by medical intervention.(1, 2) An integral part of NPT is teaching women to observe and chart the biomarkers of their fertility (menstrual) cycle, based on changes in vaginal discharge (resulting from uterine bleeding and cervical mucus production). This charting of fertility biomarkers is done according to the Creighton Model FertilityCare System (CrM). (3) The CrM has several applications. First, the CrM chart alerts women when ovulation is approaching within the next few days and therefore intercourse is most likely to result in pregnancy, even for subfertile couples.(4, 5) Second, it also gives the physician a record that can be used as a standardized basis for doing diagnostic tests timed in reference to ovulation. Third, the physician can also employ standard medications to enhance ovulation, luteal hormonal production, or cervical mucus production, and use the CrM chart to assess the immediate response of the woman to treatment. Where appropriate, NPT may also include medical treatment for male factor infertility, and for prior miscarriage. Formal evaluation of the outcomes of NPT in medical practice has been limited to a few studies based on single medical practices.(6-9) We plan to conduct a prospective observational study to measure the generalizability of this program to multiple populations and settings, and characteristics of patients that may correlate with the likelihood of treatment success.

Please save frequently

b) Describe any animal experimentation and findings leading to the formulation of the study, if there is no supporting human data.

NA

2. Purpose of the study

a) Provide a brief lay summary of the project in <200 words. The lay summary should be readily understandable to the general public.

This study involves research, and the purpose of this study is to evaluate live birth rates among couples who are treated by Natural procreative technology, (NPT) for infertility and miscarriage.

Comparisons will be made to those declining NPT treatment, waiting for NPT treatment, receiving other treatment, or stopping treatment. We seek to document specific pregnancy rates for different factors such as age and type of infertility diagnosis. We will also assess characteristics of environmental exposures that may be associated with infertility. Couples will be followed for up to three years, regardless of when they begin NPT treatment, or whether they continue treatment. We are seeking the broadest possible participation from couples who are considering NPT treatment. Data from all couples will be useful for this study, regardless of their individual circumstances or actual treatment.

Page numbers from a sponsor's protocol/grant may be referenced in 2b and 2c.

b) List your research objectives (specific aims & hypotheses of the study).

This is an exploratory study rather than a hypothesis testing study. This study aims to determine what the live birth rates are over time for patients who are treated with natural procreative technology (NPT) for infertility or history of spontaneous abortion, and how the live birth rate may vary by patient characteristics, especially the age of the woman, prior pregnancy, and underlying diagnoses. Secondary analyses will explore outcomes of conceptions (live birth versus other outcomes) and the association of environmental exposures with infertility. This is an observational study: there will be no intervention. Patients will receive whatever care they choose to receive. Couples receiving NPT treatment will be compared to those declining NPT treatment, waiting for NPT treatment, receiving other treatment, or stopping treatment. Interventions received, conceptions, and outcomes of conceptions will be followed for up to 3 years for each couple entering the study.

Please save frequently

c) **Describe the study design (e.g., single/double blind, parallel, crossover, control, experimental, observational, etc.). If the study is investigator-initiated, a timeline for individual subject recruitment, follow-up, and analysis for the study is required. Also, indicate if the subjects will be randomized.**

This is a prospective cohort observational study. Couples presenting for possible treatment with NPT will be recruited for participation in the study. No randomization will occur. If a couple agrees to participate, we will collect information in three ways:
1)Questionnaires. (This is standard of care) These will be done at entry (SOC) to the study, on an annual basis for up to three years (research related), for any pregnancy, or whenever a patient exits the study. Questionnaires may be done by mail, email, or telephone. Each questionnaire has a woman's and a man's version, except the pregnancy questionnaire, which only has a woman's version. Each questionnaire will take approximately 30-45 minutes to complete.
2)The subject's own Creighton Model fertility charts. (standard of care)
3)Information about NPT treatment and pregnancies from the medical records of their NPT physician(s). (standard of care)

d) **If subjects will be given placebo, please justify placebo use. *?HELP?***

NA

3. Study Procedures

a) N Is this project a multicenter study (i.e., same project is conducted elsewhere by a different investigator) OR does this study involve conduct of research at multiple sites?

Is SLU acting as a coordinating center for other sites OR is the SLU PI a direct recipient of a federal grant for this research? If yes, complete and attach the Supplemental Application for Coordinating Center Activities.

Will the SLU site be participating in all parts/procedures/arms of the study?

If No, explain what SLU will NOT participate in:

Please save frequently

Page numbers from a sponsor's protocol/grant may be referenced in 3b, 3c, and 3d.

b) **Describe all the procedures, from screening through end-of-study, that the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care. Specify which procedures are for research and which are standard of care. Please note: The box below is for text only. If you would like to add tables, charts, etc., attach those files in the Attachment section (#16).**

The clinical care will be performed as usual, and will not be altered by this study.
If a couple agrees to participate, we will collect information from them in three ways:
1)
For women:
The Woman's Entrance Questionnaire will be completed by the subject at the time of their initial visit or as soon as possible per SOC. Following enrollment into the study, the subject will complete the following questionnaires:
•Women's Update Questionnaire on an annual basis (from the date of completion of the Women's entrance questionnaire) for up to 3 years (research related),
•Pregnancy Outcome Questionnaire for any pregnancy (research-related),
•Women's Exit Questionnaire whenever they exit the study (research-related).
Depending on the timing of subject enrollment, any follow-up questionnaire time point which may have already occurred at the time of subject enrollment will be considered skipped.
Questionnaires may be done by mail, email or telephone. Each questionnaire will take approximately 30-45 minutes to complete.

For male partners:
The Men's Entrance Questionnaire will be completed per SOC (may be completed before or after enrollment into the study).

Following enrollment into the study, the subject will complete the following questionnaires:
•Men's Update Questionnaire on an annual basis (from the date the female partner completed the Women's entrance questionnaire) for up to 3 years (research-related),
•Men's Exit Questionnaire whenever they exit the study (research-related).
Depending on the timing of subject enrollment, any follow-up questionnaire time point which may have already occurred at the time of subject enrollment will be considered skipped.
Questionnaires may be done by mail, email, or telephone. Each questionnaire will take approximately 30-45 minutes to complete.

2)The subject's own Creighton Model fertility charts.(The Creighton Model Fertility charts teaches couples to recognize, understand, and record the changes that occur during the fertility [menstrual] cycle. These changes [biomarkers] indicate whether the reproductive system is functioning normally or not. It also identifies ovulation and other key events. It is completely natural and cooperative with a woman's fertility [menstrual] cycle).
3)Information about NPT treatment and pregnancies from the medical records of their NPT physician(s) (prospective and/or retrospective, based on the timing of consent)..

This data collection will continue for up to three years after enrollment into the study (research related).

We will keep track of all information, including information needed to contact the subject at the Study Center at Saint Louis University. All information will be kept confidential. No personal information will be released to anyone outside the study.

The study database has been constructed without any patient identifiers (no name, address, phone number, or identification numbers other than study subject number). The subject's contact information will be kept separate from the study data.

Combined results will be used for the analysis in this study. It will be impossible to identify any individual during the course of the analysis or in the reporting of the results.

Couples presenting for possible treatment with NPT will be recruited for participation in the study. Observation of the characteristics of the couples, the nature of the NPT treatments, and the outcomes including live births will be followed for up to 3 years for each couple entering the study.

The paper informed consent form will be reviewed with the couple in detail in the office. Individuals will have the opportunity to ask questions before they consent.

Follow up Questionnaires may be completed per the patient's preference, by e-mail, phone or in person.

All data collected (no PHI) from the questionnaires and medical records will be entered into a single secure database that will be kept at the Saint Louis University , Department of Ob, Gyn and Women's Health.

c) **If the proposed study is a clinical trial where a drug, vaccine, device or other treatment is compared to a placebo group or comparison treatment group, what are the guidelines or endpoints by which early decisions regarding efficacy or lack of efficacy can be made? For example, it may be reasonable to stop enrollment on a study when efficacy has already been clearly demonstrated, to avoid unnecessary enrollments of additional subjects. Alternatively, it may be reasonable to stop enrollment when it is clear that efficacy will never be demonstrated, given the statistical power of the study as designed. Describe the guidelines that are in place to assist in making these determinations, if relevant to the proposed study.**

NA

d) **Describe how data analysis will be performed (statistical tests, methods of evaluating data) and indicate the smallest group/unit for which separate reporting will occur. For studies involving a questionnaire, if data and reliability information are available, please describe or provide references. For full board, unfunded studies describe sample size determination and power analysis. If none, please justify.**

The database exists in Microsoft Access. Analyses will be done in Excel (for basis of descriptions), SAS and/or SPSS statistical computer programs. As stated above, data used in the analysis will be aggregate data, and will not contain any individual identifiers. Therefore, there will be no possibility of identifying individual respondents during the analysis or in the reporting of the final results.

Analysis of Main Outcome
The main outcome of this study is the proportion of subjects that had a live birth at various time points up to five years after beginning treatment with NPT, compared to couples who do not receive NPT treatment, or who cease to receive NPT treatment. This will be analyzed by standard lifetable techniques to deal with censored data (i.e., couples for whom pregnancy status cannot be ascertained beyond a certain time period). Cox proportional hazards regression will be used in an exploratory manner to investigate demographic and medical characteristics (particularly woman's age, prior pregnancy, and associated medical diagnoses) that may be associated with a greater likelihood of successful live birth. The same set of analyses will be repeated for the secondary outcome of conception (clinical pregnancy).

Analysis of Secondary Outcomes
Initially, all secondary outcomes will be analyzed as simple proportions, e.g., of couples who conceived, what proportion had a live birth, spontaneous abortion, or other pregnancy outcome.

conceived, what proportion had a live birth, spontaneous abortion, or other pregnancy outcome. Where indicated by the initial analysis, supplementary analyses using standard statistical techniques may be employed (e.g., a logistic regression with the outcome of live birth versus other pregnancy outcome).

Sample Size
The sample size is not exact since its size depends upon the total number of patients seen at the participating clinic. We do not have sufficiently reliable information to estimate the variance of the predictor variables (age, prior pregnancy, associate medical diagnoses, and other characteristics) in predicting the primary outcome of live birth. Because this is an observational study of existing treatment, we will conduct interim analyses yearly.

Please save frequently

e) **State if deception (including incomplete disclosure of study purpose/procedures) will be used. If so, describe the nature of the deception and provide a rationale for its use. Also, describe debriefing procedures or justify a waiver of the requirement to debrief. NOTE: for studies using deception, an alteration of consent must be justified in the Informed Consent section of the protocol (#13) and the debriefing script/statement must be uploaded in the Attachments section (#16). See IRB Deception Guidelines.**

f) **Is there an accepted standard of care and/or standard practice at SLU for the condition/disease/situation being studied? This information will assist in comparing the risk/benefit ratio of study procedures relevant to usual care that would be received outside of the research context. *?HELP?*** Y

If yes, please describe the standard of care and standard practice at SLU for the condition/disease/situation being studied.

NPT incorporates standard infertility treatments (such as clomiphene or progesterone) within a set of standardized application protocols. The goal of NPT is to identify abnormalities of the woman's reproductive cycle (menstrual cycle), and where possible, correct them by medical intervention.(1, 2) An integral part of NPT is teaching women to observe and chart the biomarkers of their fertility (menstrual) cycle, based on changes in vaginal discharge (resulting from uterine bleeding and cervical mucus production). This charting of fertility biomarkers is done according to the Creighton Model FertilityCare System (CrM). (3) The CrM has several applications. First, the CrM chart alerts women when ovulation is approaching within the next few days and therefore intercourse is most likely to result in pregnancy, even for subfertile couples.(4, 5) Second, it also gives the physician a record that can be used as a standardized basis for doing diagnostic tests timed in reference to ovulation. Third, the physician can also employ standard medications to enhance ovulation, luteal hormonal production, or cervical mucus production, and use the CrM chart to assess the immediate response of the woman to treatment. Where appropriate, NPT may also include medical treatment for male factor infertility, and for prior miscarriage.

g) **Does this study involve any diagnostic imaging, labwork or genetic testing that could result in clinical discovery (diagnoses, genetic mutations, etc.)? Note that this could include discovery that is expected (related to the research) or incidental (not related to research aims, but possible, like a mass/shadow found in imaging despite not looking for it).** N

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If yes, please describe and include whether there are plans to share findings with study participants.

h) **Is this study subject to the NIH Genomic Data Sharing Policy?** N

The NIH GDS policy applies to all NIH-funded research that generates large-scale human genomic data as well as the use of these data for subsequent research and includes: genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomics, epigenomic and gene expression data, irrespective of NIH funding mechanism. Click here for more specific examples.

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* * * Radioisotopes or Radiation Machines * * *

You have not selected the Radioisotopes option in the General Checklist. If you would like to add Radioisotopes information, please select the option to enable this section.

4. Radioisotopes or Radiation Machines

In this section, investigators must enter all radiation usage associated with the protocol.

Important: Protocols that involve non-standard of care radioactive materials (which includes the terms "radioisotopes", "radionuclides", "radiopharmaceuticals", and "nuclear medicine studies", e.g., "PET", "MUGA", "Zevalin", and/or specific radionuclides such as "F-18", "Tc-99m", "Th-201", "I-131", "Ra-233", "Y-90", etc.) will receive review by the Radiation Safety Officer (RSO) and/or Radiation Safety Committee (RSC). In these cases, submission to the RSO/RSC should occur after the IRB staff has drafted the informed consent radiation exposure risk statement, or verified the statement that was drafted by the research team (as noted below*). For more information on how to submit for radiation safety review, see RSC instructions or contact the Radiation Safety Officer at 977-6895.

(1) It is the responsibility of the PI to assure the accuracy and completeness of the data submitted in this section, consistent with guidelines provided below. (2) For projects requiring radiation procedures, please refer to this guidance.

a) **If applicable, list and quantify the radiographic diagnostic and therapeutic procedures associated with this protocol by clicking "Add" and adding to Table 1 below. (Includes X-ray, fluoroscopy, CT, radioactive materials, nuclear medicine, PET-CT, radiation oncology, accelerator, Cyber Knife procedures, etc.)**

b) **Total estimated research radiation dose * :**

* Calculate from the table above by adding the Effective Dose Subtotals for all procedures.

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*NOTE: Informed Consent Radiation Exposure Risk Statement- The appropriate Informed Consent Radiation Exposure Risk Statement template language must be inserted into the SLU IRB Informed Consent, inclusive of applying the total estimated research radiation dose specified in item b) from the table above, as instructed in the SLU IRB Informed Consent Template. Per IRB Guidelines, the language will either be drafted by the IRB staff or drafted by the research team and then verified by IRB staff prior to submission to the RSC for review. Contact the IRB Office at 977-7744 or irb@slu.edu with any questions.

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* * * Devices * * *

5. Devices

a) Please list in the space below all investigational devices to be used on subjects during this study.

b) Please list in the space below all FDA approved devices to be used on subjects during this study.

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* * * Drugs, Reagents, Chemicals, or Biologic Products * * *

6. Drugs, Reagents, Chemicals, Biologic Products, or Dietary Supplements, Vitamins, and Other Food Agents

Pilot	Phase I	Phase II
Phase III	Phase IV	X Not Phased

List placebo if it is considered a drug (contains more than inactive ingredients). For example, normal saline is considered a drug that should be listed, whereas placebo tablets are usually inert ingredients that do not need to be listed.

b) Please list in the space below all investigational drugs, reagents or chemicals to be administered to subjects during this study. Attach all applicable Investigator Brochures in section #16 (Attachments).

c) Please list in the space below all FDA approved drugs, reagents, chemicals to be administered to subjects during this study. Attach all applicable package inserts in section #16 (Attachments).

d) Please list in the space below all dietary supplements, vitamins, minerals, or foods to be administered to subjects during this study.

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* * * Other Levels Of Review * * *

7. Other Levels Of Review

1. University Radiation Safety

Protocols that involve non-standard of care radioactive materials (which includes the terms "radioisotopes", "radionuclides", "radiopharmaceuticals", and "nuclear medicine studies", e.g., "PET", "MUGA", "Zevalin", and/or specific radionuclides such as "F-18", "Tc-99m", "Th-201", "I-131", "Ra-223", "Y-90", etc.) will receive review by the Radiation Safety Officer (RSO) and/or Radiation Safety Committee (RSC). For information on how to submit for radiation safety review, see RSC <a href=https://www.slu.edu/research/faculty-resources/research-integrity-safety/documents/irb-protocols-requiring-rsc-review-instructions-for-coordinators.pdf target=_blank > instructions or contact the Radiation Safety Officer at 977-6895.

X **Not Applicable**

Yes, study involves radioactive materials

2. Institutional Biosafety

Experiments involving the deliberate transfer of Recombinant or Synthetic Nucleic Acid Molecules (e.g., Gene Transfer), or DNA or RNA derived from Recombinant or Synthetic Nucleic Acid Molecules, or Microorganisms containing Recombinant or Synthetic Nucleic Acid Molecules and/or infectious agents (including select agents and toxins as defined by CDC and/or Animal and Plant Health Inspection Service (APHIS)) into one or more human research participants must be reviewed by the SLU Biological Safety Officer. Most of these protocols also require review and approval by the SLU Institutional Biosafety Committee (IBC). Please contact the SLU Biological Safety Officer at 977-6888 for more information.

X **Not Applicable**

Yes, study requires Institutional Biosafety review

3. Pharmacy, Therapeutics, Nutrition, and Transfusion (PTNT) Committee

Saint Louis University Hospital requires that all research involving the administration of medications within the hospital (including outpatient areas such as the Emergency Department, Outpatient Center, Saint Louis University Hospital-South Campus, etc.) be reviewed and approved by the Pharmacy, Therapeutics, Nutrition, and Transfusion (PTNT) Committee and that study drugs are received, stored, prepared, and dispensed by the Hospital's Department of Pharmacy Services. Please contact the Investigational Drug Services Clinical Pharmacist at 268-7156 or SLUH-IDS@ssmhealth.com for more information.

X **Not Applicable**

Yes, study requires PTNT review

4. Saint Louis University Hospital

All research involving Saint Louis University Hospital, including the Emergency Department, inpatient or outpatient services (including outpatient surgery at SLUH South Campus and the infusion center at the DOB) and medical record access, requires Research Business Review (RBR) and approval prior to study initiation. This process is designed to facilitate compliance with state and federal regulations as they pertain to research in hospitals and clinical research billing. While researchers can begin to complete the SSM RBR form at any time, the form should not be submitted until the IRB and the Clinical Trials Office (CTO) have approved the study. Please contact the Research Compliance Office at 577-8113 or sluh-research@ssmhealth.com or the CTO at 977-6335 or clinical-trials-office@health.slu.edu for more information.

X Not Applicable

Yes, study requires Saint Louis University Hospital review

5. SSMSL

All research involving SSMSL locations (including Cardinal Glennon), including inpatient or outpatient services and medical record access, requires approval from the SSM STL or SSM Cardinal Glennon Research Business Review (RBR) prior to study initiation. This process is designed to facilitate compliance with state and federal regulations as they pertain to research in hospitals and clinical research billing. While researchers can begin to complete the SSM RBR form at any time, the form should not be submitted until the IRB and the CTO have approved the study. Please contact the SSMSL Office at 989-2058 or Marcy.Young@ssmhealth.com for more information.

X Not Applicable

Yes, study requires RBR review

6.   Does this project require registration on ClinicalTrials.gov, and/or is this project subject to the NIH GCP Training Requirement? (Select "Yes" if either apply) Y

Registration may be required if any of the following apply: 1) The project meets the FDAAA definition of an "Applicable Clinical Trial", which requires registration on ClinicalTrials.gov. 2) As of January 1, 2017, a new NIH policy mandated biomedical and behavioral "Clinical Trials" to be registered on ClinicalTrials.gov. In addition, NIH policies require personnel on NIH "Clinical Trials" to take GCP training every three years. 3) Registering may be required for Journal Publication (ICMJE). Please review relevant definitions here. Contact the CTO at clinical-trials-office@slu.edu with questions about registering on ClinicalTrials.gov and refer to the training page of the IRB website for information on NIH GCP Training requirements.

* * * Subject Population * * *

8. Subject Population - In the space below, please detail the participants that you are requesting to recruit

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(include description of each group requested)

a) **Expected age range of subjects. (For example ≥ 18 yrs to 90 yrs).**

18-55yrs of age

b) **Number of evaluable subjects to be accrued at SLU or SLU site (this includes all sites under the direction of the SLU PI).** 600 participants (300 women and 300 partners)

Exceeding the number listed here is a protocol violation. Prior IRB approval is required if additional participants are to be accrued. If applicable, this number should be consistent with your power analysis described in 3d.

c) **Number of evaluable subjects to be accrued study wide. *?HELP?*** 600 participants (300 women and 300 partners)

d) **If including vulnerable populations (minors, pregnant women and fetuses, neonates, non-English speaking, economically or educationally disadvantaged, prisoners, adults temporarily or permanently unable to consent for themselves): 1) provide the rationale for the importance of including this population in the research, and 2) specify the measures being taken to minimize risks to potentially vulnerable subjects. Click on hyperlinks to access SLU Guidelines containing additional considerations and strategies for mitigating risks.**

NA

e) **If women, minorities, or minors are not included, a clear compelling rationale must be provided unless not applicable. Examples for not including minors: disease does not occur in children; drug or device would interfere with normal growth and development; etc. If federally funded reference appropriate section of the sponsors protocol/grant. *?HELP?***

Women and minorities are included. Usually minors are not seen for infertility

f) **If any specifically targeted subjects are students, employees, or laboratory personnel, specify the measures being taken to minimize the risks and the chance of harm to these potentially vulnerable subjects. See SLU Guidelines for additional considerations and strategies for mitigating risks.**

g) **Describe (labeled a-c): a) who you are recruiting for this study (e.g., your patients/students/colleagues, those in existing database or registry, the general public), and b) how you are recruiting (flyers, advertisements, direct call/mailing, membership networks, in-person recruitment in clinic, classroom, public locations, etc.). For secondary data analysis or specimen studies, state how you have access to materials. Importantly: do not contact participants prior to obtaining IRB approval for your study.**

c) Also indicate whether or not you plan to obtain personal/private information or biospecimens for the purpose of screening, recruiting, or determining eligibility of prospective subjects prior to obtaining informed consent and how (obtained by communicating with prospective subjects or obtained by accessing records or stored biospecimens). Note: if you are accessing medical records other than those of your own patients or those in your immediate department, you will need to submit a <a href= https://www.slu.edu/research/faculty-resources/research-integrity-safety/institutional-review-board-irb/irb_assets/prep_to_research_form.doc target=_blank>HIPAA Preparatory to Research form and submit to the SLU Privacy Officer PRIOR to accessing records.

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Please refer to the <a href=https://www.slu.edu/research/faculty-resources/research-integrity-safety/institutional-review-board-irb/irb_assets/guidelines_subject_recruitment.doc target=_blank>SLU IRB Recruitment Guidelines when designing recruitment strategies and upload recruitment materials to the Attachments page for IRB review. You are expected to obtain permission for individuals/organizations that assist with recruitment, and whenever possible, those assisting should share your materials with potential participants on your behalf rather than providing you with private contact information.

Couples seeking NPT treatment or consultation to achieve pregnancy, to maintain pregnancy, or for fertility-related health issues will recruited from our practice. Providers will present the study information to the patients at any visit. Women and their partner do not have to be consented at the same visti/on the same date. No recruitment by phone or mail will be done.

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* * * Subject Population * * *

8. Subject Population (continued)

Page numbers from a sponsor's protocol/grant may be referenced in 8h.

h) **Inclusion and Exclusion Criteria.**

Identify inclusion criteria.

1.Couple or women, seeking NPT treatment or consultation to achieve pregnancy, to maintain pregnancy, or for fertility-related health issues.
2.Couple or women who is seeking pregnancy WITHIN the coming year.

Identify exclusion criteria.

1.Couple or women is not a candidate for NPT for pregnancy (for example, couple or women is medically sterile or medically too high risk for pregnancy).
2.Couple or women is not able to provide informed consent (for example, language barriers).

i) **Compensation. Explain the amount and schedule of compensation, if any, that will be paid for participation in the study. Include provisions for prorating payment.**

No compensation will be paid

j) **Describe who will cover study related costs. Explain any costs that will be charged to the subject.**

Neither the subject or their insurance company will be billed for any study related procedures.

k) **Estimate the probable duration of the entire study including data analysis and publication. This estimate should include the total time each subject is to be involved and the duration the data about the subject is to be collected. If the study is Investigator-initiated, a timeline for individual subject recruitment, follow-up, total time for subject accrual, and data analysis for the study is required.**

Annual questionnaires will be sent out to consented participants yearly for 3 years
We anticipate keeping the study open for up to 10 years for enrollment.
Couple/Female involvement 3 years
Data collection per couple 3 years
Analysis and publication 3 years
Total duration of study 19 years

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* * * Risks * * *

9. Risks

There is no research that can be considered totally risk free (e.g., a potential risk of breach of confidentiality). Therefore, when describing the risk, the lowest level of risk is "no more than minimal risk".

Page numbers from a sponsor's protocol/grant may be referenced in 9.1, 9.2, 9.3, and 9.4.

1. **Use of investigational devices. Please include the clinical adverse events (AEs) associated with each of the devices with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with procedures that subjects may experience while in the study.**

2. **Use of investigational drugs. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with placebos or washout periods that subjects may experience while in the study.**

3. **Use of FDA approved drugs, reagents, chemicals, or biologic products. Please include the clinical AEs associated with each of the drugs with an indication of frequency, severity and reversibility. This information can often be found in the package insert provided by the manufacturer. NOTE: Include any likely adverse effects associated with placebos or washout periods that subjects may experience while in the study.**

4. **Use of FDA approved devices. Please include the clinical adverse events (AEs) associated with each of the devices with an indication of frequency, severity and reversibility. This information can often be found in the Investigator(s) brochure. NOTE: Include any likely adverse effects associated with procedures that subjects may experience while in the study.**

5. **Describe any risks related to performing study procedures. Please include all investigational, non-investigational, and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).**

There is the risk of loss of confidentiality.

6. **Describe any risks related to the use of radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy).**

7. **Describe why this investigational compound/drug/device/procedure's risks/benefits are potentially better than standard of care or other common alternatives. Any standard treatment that is being withheld must be disclosed and the information must be included in the consent form. *?HELP?***

This Study is solely observational– it evaluates clinical treatment that is being provided already and involves no additional drugs or interventions. No care or treatment is being withheld.

8. **Describe any psychological, social, or legal risks the subject may experience. *?HELP?***

There are certain risks and discomforts that may occur if a patient takes part in this research study. These include the potential risk of loss of confidentiality. Every effort will be made to keep the information confidential, however, this cannot be guaranteed.

Some of the questions on the questionnaire may make participants feel uncomfortable. They may refuse to answer (skip) any questions.

Page numbers from a sponsor's protocol/grant may be referenced in 9.9 and 9.10.

9. **Special Precautions. Describe the planned procedures for protecting against or minimizing potential risks. If appropriate, include the standards for termination of the participation of the individual subject. Discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.**

Data collected will be coded, stored in a locked suite, on a password protected computer. The master list will be kept separately from the data collected.

PHI information will be stored with the coded study information. Documents such as the consent (name) Demographic sheets from the SOC contains PHI. All study related documents will be stored in a locked cabinet (only the data manager has the key) in a locked suite.

The subject couple information will be entered into the database housed by the Department of Ob, Gyn and Women's Health at Saint Louis University

The study database will be constructed without any patient identifiers (no name, address, phone number, or identification numbers other than study subject number). Study subject numbers will be linkable to individual patients only at Saint Louis University. The data file will be password protected, and located on a password-protected computer in a locked research area of the Department of OB, GYN and Women's Health. Combined results will be used for the analysis in this study. It will be impossible to identify any individual during the course of the analysis or in the reporting of the results.

10. **Reproductive Risks.**

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a. **Please list the pregnancy category of any drugs or N/A.**

na

b. **Please describe any reproductive risk associated with any part of the research study. Include any data from other studies (animal or human).**

na

11. **Data Safety Monitoring**

Federal regulations require that when appropriate, the research protocol makes adequate provisions for monitoring the data to ensure the safety of participants. Monitoring should be commensurate with risks and with the size and complexity of the research, and could range from no plan needed to an independent data safety monitoring board. Please refer to SLU Guidelines for Data and Safety Monitoring as you complete the questions below.

a. Is there a Data Monitoring Committee (DMC) or Board (DSMB)? N

If yes, please provide the following information (labeled a-g): a) the composition of the board (degrees/qualifications of members), b) whether the board is independent from the sponsor and research team or not, c) frequency of meetings and issuance of reports to sites, d) assurance that the board is reviewing aggregate safety data and making recommendations regarding study continuance, e) provisions for ad hoc meetings if needed, f) who is reviewing SAEs in real time (MD or DO), and g) stopping/halting rules (if any exist).
A DSM charter can be referenced for all items except for "f) who is reviewing SAEs in real time."

If no, please justify why not.

Not needed, this is an observational study

b. Is there a Data Safety Monitoring Plan (DSMP)? N

Note, if all relevant plan information is included in DSMB question above, select 'Yes' and state "see above" in the answer box.

If yes, provide details (labeled a-e) including: a) what types of data or events are captured and how are they documented, b) who is monitoring data, their independence/affiliation with the research and their degrees/qualifications, c) frequency of aggregate data review, d) who is reviewing SAEs in real time (MD or DO), and e) stopping/halting rules (if any exist).

If no, please justify why not.

Not needed, this is an observational study

12. **In case of international research (research outside of the U.S. or research on international populations (non-U.S.)), describe qualifications/preparations that enable you to evaluate cultural appropriateness and estimate/minimize risks to subjects. Include whether research is sensitive given cultural norms.**

a. **State any local laws/regulations governing Human Subjects Research in the country(ies) you will conduct the research and attach any relevant approvals. If none, state N/A.**

b. **Will there be language barriers and if so, how will they be addressed?**

Note: If materials are to be distributed to subjects in their native language, please follow SLU's Guidance For Studies Involving Non-English Speaking Subjects.

         NOTE: Export control laws include the transfer of technical information and data, as well as information
         and technology to foreign nationals. If this study has international components, contact the SLU Export
         Control Officer for direction on whether export control policies apply.

* * * Benefits/Alternatives, Procedures to Maintain Confidentiality and Privacy * * *

10. Benefits/Alternatives

a) **Benefits. Describe the potential benefit(s) to be gained by the subjects and how the results of the study may benefit future subjects and/or society in general. Indicate if there is no direct benefit to the participants.**

Subject participation may not benefit them but may help generate information about specific pregnancy rates and outcomes that will benefit future couples considering NPT treatment.

b) **Alternatives. Describe any alternative treatments and procedures available to the subjects should they choose not to participate in the study. If no such alternatives exist, please state that the alternative is nonparticipation. For some studies, such as record reviews, a description of alternatives would not be applicable.**

The alternative to participating in this study is not to participate. Whether or not subjects enroll in this study will not change the NPT treatment that they receive, or choice to pursue any other treatment

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11. Procedures to Maintain Confidentiality and Privacy

Federal regulations require that research materials be kept for a minimum of three (3) years and HIPAA documents be kept for a minimum of six (6) years after the closure of the study. For FDA-regulated or sponsored projects, the PI may be required to keep the data and documents for a longer time period.

Confidentiality

To determine whether adequate provisions for confidentiality of data are in place, the IRB must ensure that research materials are stored in appropriate locations throughout the study (during collection, transport/transmission, analysis and long term storage). Research information must be protected using appropriate safeguards based on identifiability of the data and risk associated with the study (See SLU IRB Confidentiality Guidelines).

For the questions below, please use the following definitions:

Anonymous/De-identified: data contain no identifiers, including code numbers that investigators can link to individual identities;

Coded: data in which (1) identifying information, such as name or social security number, has been replaced with a number, letter, symbol, or combination thereof (i.e., the code), and (2) a key to decipher the code exists enabling linkage of data to identifying information (e.g., a master list), and (3) the key (master list) is kept separately from coded data; AND/OR

Identifiable: data that includes personal identifiers (e.g., name, social security number), such that information could be readily connected to respective individuals.

a) **Electronic (Computer) Data**

Click "Add" to enter data security information for each type of electronic data that will be created in the study: anonymous/de-identified, coded, and/or identifiable (see definitions above).

To properly address this question, there should only be one listing of each type of data in the table. Depending on your project, you could have up to three types of data. See the SLU ITS Sensitive Data Guide for acceptable data security methods.

Not Applicable, No Electronic (Computer) Data

X Study IRB-approved Prior to New Question (Question N/A- Grandfathered)

b) **Hardcopy (Paper) Data**

Click "Add" to enter information for each type of hardcopy (paper) data that will be created in the study: anonymous/de-identified, coded, and/or identifiable (see definitions above).

To properly address this question, there should only be one listing of each type of data in the table. Depending on your project, you could have up to three types of data.

Not Applicable, No Hardcopy (Paper) Data

X Study IRB-approved Prior to New Question (Question N/A- Grandfathered)

c) **If a master list is used in this study (linking study codes to subject identifiers), explain: a) how and where you will secure the master list, b) how long it will be kept/when it will be destroyed, and c) provide a sample of the code.**

Data will be stored on a secure, password-protected server or computer. The informed consent will be stored in a locked file cabinet, behind locked doors in the Research Unit.

A master list will be kept separately from the data. The master list is necessary in the event that data collected needs to be confirmed or is questioned and to correlate reports to the correct subjects and to contact subjects for annual questionnaires. It will be kept until study is complete and results published then it will be destroyed.

d) **If data or specimens are being shared outside of the research team, indicate who will receive the material, specifically what they will receive (data or specimens), and if an agreement has been signed to cover the transfer. Note: unless covered under a Clinical Trial or other agreement, the transfer of data or specimens to an external entity will require an agreement. For the transfer of materials (specimens), a Materials Transfer Agreement (MTA) is used; for the transfer of data, a Data Use or Data Transfer Agreement is used. Please contact the Research Innovation Group at 314-925-3027 for assistance.**

na

e) **If samples or data will be provided to SLU from an outside source, indicate whether you will have access to identifiers, and if so, how identifiable information is protected. Note: unless covered under another agreement (e.g., Clinical Trial Agreement or subcontract), the transfer of data or specimens from an external entity to SLU may require an agreement. For the transfer of materials (specimens), a Materials Transfer Agreement (MTA) may be required; for the transfer of data, a Data Use or Data Transfer Agreement may be required. Please contact the Research Innovation Group at 314-925-3027 for assistance.**

NA

f) **If data will be collected via e-mail or the Internet, how will anonymity or confidentiality be affected? Describe how data will be recorded (i.e., will internet protocol (IP) addresses and/or e-mail addresses be removed from data?).**

Each participant will have their own username and password if they choose to complete the questionnaire on line.
If they choose to have the questionnaire mailed to them, a stamp returned envelope will be provided with the participant's code number noted on the questionnaire.
If they wish to complete the questionnaire over the phone an approved member of the research team will contact them and complete the questionnaire with a code number identifying the participant.

g) If you will be audio/video recording or photographing subjects, provide a rationale as voiceprints and images of faces/unique body markings are considered identifiers. Describe confidentiality procedures, including any restricted access to images and/or the final disposition of the recordings/photos (destruction, archiving, etc.).

h) Describe any study-specific (non standard of care) information or documentation that will be put in the participants' medical records for this research (e.g., study visit notes, lab results, etc.). If none, state "not applicable". NOTE: documentation of research in Epic should be done in accordance with the SLUCare Epic Research Charting Policy and Clinical Workflow: Documenting Research Encounters in Epic.

Nothing will be recorded

i) Are there any information security requirements identified in the project's RFP/Award Notice/Contract? This could include data security, technical safeguards, security controls, NIST, FISMA, CFR, etc. N

If yes, SLU ITS approval is required. Contact InfoSecurityTeam@slu.edu to start the approval process.

Privacy

Privacy refers to persons having control over the sharing of oneself with others.

j) Please indicate how participant privacy will be protected in this study (select all that apply):

- X Discussion of health related and/or personal information in a private room/area
- X Research interactions/interventions are conducted in a private room/area
- Use of drapes or other privacy measures
- X Collection of sensitive/identifiable information is limited to the minimum necessary to achieve the aims of the research
- X Access to study information is limited to the minimum amount of persons necessary to achieve the aims of the research (e.g., access restricted to research team members only)
- Consideration of parental inclusion/absence for studies involving minors
- Other (please explain):

Protocol Title: Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

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* * * Potential Conflict of Interest * * *

12. Potential Conflict of Interest

Indicate whether you, your spouse or dependent children, have, or anticipate having, any income from or financial interest in a sponsor, device or drug manufacturer of this protocol, or a company that owns/licenses the technology being studied. Please remember that you are responding for you and any other investigator participating in the study. Financial Interest includes but is not limited to: consulting; speaking or other fees; honoraria; gifts; licensing revenues; equity interests (including stock, stock options, warrants, partnership and other equitable ownership interests). For questions regarding Conflict of Interest consult the Conflict of Interest in Research Policy.

Check one of the following (please remember that you are responding for yourself, your spouse, dependent children and any investigator, investigator's spouse and dependent children participating in the study):

1) X **No equity interest and/or Financial Interest less than or equal to $5K**
2) **Any equity interest and/or Financial Interest exceeding $5K but not exceeding $25K in the past year or expected in the current year**
3) **Financial Interest exceeding $25K in the past year or expected in the current year**

Check all those that apply:

Consulting
Speaking Fees or Honoraria
Gifts
Licensing agreement or royalty income
Equity interests, (including stock, stock options, warrants, partnership or equitable ownership interests), or serving on a scientific advisory board or board of directors
Other fees/compensation

If you have marked #2 or #3, please contact coi@slu.edu to initiate review of this study and provide the following information:

1. A Conflict of Interest Management Plan.
   has been approved for all investigators for this study
   is pending
   has not been initiated

2. Describe who has, and briefly explain, the conflict of interest and indicate specific amounts for each subcategory checked:

Protocol Title: Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

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Note to Investigator(s) Reporting a Potential Conflict of Interest

Investigator(s) must have:

1. Current, up-to-date Conflict of Interest Disclosure Form on file with the SLU Conflict of Interest in Research Committee (COIRC) that describes any financial relationship indicated above.

   - This information must be disclosed on the SLU confidential Conflict of Interest Disclosure Form and reviewed by the COIRC before accruing research subjects in this study. If your current Disclosure Form does not contain this information, you are required to submit an updated Disclosure Form to the COIRC.

2. You may not begin your study until your disclosure form has been reviewed and any required management plan has been approved by the COIRC for this study. To initiate COIRC review of your study, please contact coi@slu.edu.

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* * * Informed Consent * * *

13. Informed Consent

Federal regulations require that informed consent be obtained from individuals prior to their participation in research unless the IRB grants a waiver of consent. Answer the questions, below, then click Add to provide the necessary consent documents and information regarding subject consent. Multiple consents/waivers may be added, but they must be uploaded one at a time.

NOTE: You may refer to the SLU IRB Guidance for Obtaining Informed Consent for considerations regarding the consent/assent process.

State N/A if not applicable.

1) **How is consent being obtained? When and where will the discussion take place? If the study involves a Non-English Speaking participant/population, please include details about plans for translated consent materials and interpreters to be used (see SLU Guidelines for Involving Non-English Speaking Subjects for more details).**

Consent will be obtained by a member of the research team at the time the subject is evaluated at their initial consultation or at any subsequent visit. If consent is obtained by a non-medical member of the research team, a medical member of the team will be available to answer the subject's medically related questions

2) **If the study involves adults unable to consent for themselves (whether diminished capacity to consent is temporary, permanent, progressive or fluctuating), please address the following: a) how is capacity to provide consent being assessed (initially and throughout study, if applicable); b) if unable to provide consent, how is LAR being determined (See SLU LAR Guidelines); c) if unable to provide consent, will assent be obtained and if not, why not?; d) if unable to provide assent, will dissent be honored and if not, why not? Note: participants initially unable to provide consent for themselves are expected to be given an opportunity to provide consent once capacity is gained. See SLU Guidelines**

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for Adults Unable to Provide Consent for additional detail.

NA

Note: Any assent documents which will be used per the Adults Unable to Provide Consent guidance, should be appropriately named and uploaded using the Add button and the Consent drop down menu selection.

Informed Consent

Title	Consent Type	Attached Date
Approved_ Marked Main ICF Version 5 CR 2017 16-JA...	Consent	01/19/2018

*** Assent ***

14. Assent

Complete this section if your study includes minors. The Assent Form Templates (For children and For adolescents) provide guidelines for writing the assent document.

1. Will minors be asked to give assent, then consent once they reach adulthood? If not, please justify. If not capable to provide assent initially, please address whether assent will be obtained as the minor gains capacity. Note: children who reach the age of adulthood during participation should be given the opportunity to provide consent as parent/guardian consent no longer applies. If obtaining consent would be impracticable (e.g., this is a registry with data/specimen obtained long ago), a waiver of consent should be added for IRB review. See SLU Guidelines for Research Involving Minors for additional detail.

2. If minors are asked to assent and do not wish to participate, will they still be accrued in the study? If yes, justify.

3. How will the minor's ability to give assent be assessed? (Consider the age and maturity of the minors as well as their physical or mental condition). If capacity is fluctuating, please explain how capacity will be assessed throughout the study.

Note: For studies that require a discussion about reproductive risks, note that the conversation with the minor should take place separately from the parents. Also, if a minor will reach adulthood (18 in Missouri) during the course of the study, they will need to be asked to consent as an adult at that time to continue in the study.

*** HIPAA ***

15. HIPAA

Studies that access, receive or collect protected health information (PHI) are subject to HIPAA regulations. PHI is health information with one or more personal identifiers. For more information refer to the SLU IRB HIPAA Guidance.

1. **Will health information be accessed, received or collected?**

   No health information. HIPAA does not apply.

   X Yes (continue to question 2).

2. **Which personal identifiers will be received or collected/recorded?**

   No identifiers. I certify that no identifiers from the list below will be received or collected and linked to health information. (Skip remainder of page).

   Limited identifiers will be received or collected/recorded (study will likely require a data use agreement). Select Data Use Agreement- INTERNAL or Data Use Agreement- EXTERNAL as appropriate, below.

   City/State/Zip codes

   Person-specific dates (e.g., date of birth, dates of service, admission/discharge dates, etc.)

   Age (if subjects are 90+ years)

   At least one direct identifier will be received or collected/recorded.

   X Names

   Social Security numbers

   X Telephone numbers

   Linkable code or any other unique identifying number (note this does not mean the unique code assigned by the Investigator(s) to code the research data)

   X All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000

   X All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

   Fax numbers

   X Electronic mail addresses

   Medical record numbers

   Health plan beneficiary numbers

   Account numbers

   Certificate/license numbers

   Vehicle identifiers and serial numbers, including license plate numbers

   Device identifiers and serial numbers

   Web Universal Resource Locations (URLs)

Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice prints
Full face photographic images and any comparable images

If you are receiving or collecting/recording health information and at least one personal identifier, please continue to complete the sections, below.

3. Sources of Protected Health Information:

- X Hospital/medical records for in or out patients
- X Physician/clinic records
- X Laboratory, pathology and/or radiology results
- Biological samples
- X Interviews or questionnaires/health histories
- Mental health records
- Data previously collected for research purposes
- Billing records
- Other

Please describe:

4. If data will be shared outside the research team and the study involves PHI indicate how the research team will share the information.

Not applicable (continue to question 5).

Only linkable code that can link data to the identity of the subject. A code access agreement or business associate agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below.

Limited identifiers: Zip codes, dates of birth, or other dates only. The study qualifies as a Limited Data Set. A data use agreement may be needed when data are shared with other non-SLU entities. If necessary, the agreement can be added and uploaded in item #5, below, using DUA-external option.

X With unlimited identifiers. The consent document and HIPAA Authorization form must describe how the information will be disclosed.

5. HIPAA Documentation is required for this study. Use the table below to add HIPAA Documents for your study.

HIPAA Documents

HIPAA Documents	Title	Attached Date
HIPAA Authorization	Approved_HIPAA Ver 2	02/17/2016

Protocol Title: Natural Procreative Technology Evaluation and Surveillance of Treatment for Infertility and Miscarriage

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*** Attachments ***

16. Attachments

In this section, please upload additional documents associated with your protocol. Failure to attach files associated with the protocol may result in the protocol being returned to you.

Possible documents for this protocol could include:

- **Bibliography**
- **Cooperating Institution's IRB Approval**
- **Data Collection Sheet**
- **Debriefing Script**
- **Device Information/Documentation**
- **Grant Proposal/Sub-Contract**
- **Human Subjects Training Certificate/Proof of Training**
- **Information Sheet/Brochure**
- **Interview/Focus Group Questions**
- **Investigator's Brochure**
- **Letter of Agreement/Cooperation**
- **IND Application Letter**
- **Package Insert**
- **Patient Diary Form**
- **Questionnaire/Survey**
- **Recruitment Material (e.g., flyers, ads, e-mail text)**
- **Safety Information (DSM Information)**
- **Scientific/PPC Review or Department Chair Review**
- **Sponsor's Protocol**
- **Sponsor's Protocol Amendment**
- **Study Design Chart/Table**
- **Other files associated with the protocol (most standard formats accepted: pdf, jpg, tiff, mp3, wmv, etc.)**

To update or revise any attachments, please delete the existing attachment and upload the revised document to replace it.

Document Type	Document Name	Attached Date	Submitted Date
Bibliography	References	01/13/2016	01/13/2016
Data Collection Sheet	Approved_Pregnancy Outcome collection sheet	02/17/2016	02/17/2016
Data Collection Sheet	Approved_Chart Abstraction Forms V10	02/17/2016	02/17/2016

Other	Approved_e-mail	02/17/2016	02/17/2016
Other	Approved_Mail letter	02/17/2016	02/17/2016
Phone Script	Approved_Phone script	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT Men's Exit v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT MensEntQnaire v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT MensUpdate v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT WomenExitV6 v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT Womens-EntQnaire v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_NPT WomenUpdate v2	02/17/2016	02/17/2016
Questionnaire/Survey	Approved_Preg_outcomes v2	02/17/2016	02/17/2016
Other	26221 NPT Consent Review 20-JUN-2017 To IRB	01/04/2018	01/09/2018
Other	Letter IRB# 26221 and 20900 23 JUN 2017-1	01/04/2018	01/09/2018
Human Subjects Training Certificate/Proof of Training	Treiman, Sierra _Biomedical	01/04/2019	01/04/2019
Human Subjects Training Certificate/Proof of Training	Voltz, John_biomedical	01/04/2019	01/04/2019

* * * PI Obligations * * *

PI Obligations

By clicking the box below you indicate that you accept responsibility for and will follow the ethical guidelines set forth by the Belmont Report, Declaration of Helsinki, the Nuremberg Code, and the Ethical Principles of the American Psychological Association (if applicable) for the research described. It also indicates that you have the requisite funding, credentials, training, and any necessary hospital privileges, if needed, to carry out all procedures and treatments involved in the protocol.

Clicking the box also affirms that the activities involving human subjects will not begin without prior review and approval by the Institutional Review Board, and that all activities will be performed in accordance with state and federal regulations and Saint Louis University's assurance with the Department of Health and Human Services. The PI assures that if members of the SLU research team access protected health information (PHI) from a covered entity in order to seek consent/authorization for research or to conduct research, such access is necessary for the research, is solely for that purpose, and the information will not be removed from the covered

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entity without IRB authorization or approved waiver. PI further assures that the SLU research team will comply with the terms of a Data Use Agreement to PHI (if any).

1) Have you completed the annual Conflict of Interest in Research Disclosure Form? Y

You can only select N/A if you are not currently listed on any externally funded research projects nor listed on any proposals for externally funded research support.

NOTE: An annual disclosure must be completed by all faculty, staff and students involved in the design, conduct or reporting of externally funded research applications and awards.

2) Have your financial interests changed significantly since you completed the annual disclosure form? N

The PRINCIPAL INVESTIGATOR certifies that he/she has read the University's Conflict of Interest Research Policy and has checked the appropriate box in the 'Potential Conflict of Interest' section of the application. In addition, the PRINCIPAL INVESTIGATOR certifies that, to the best of his/her knowledge, no person working on this project at SLU has a conflict of interest or if a conflict of interest does exist, that an appropriate management plan is in place.

According to the Saint Louis University Conflict of Interest in Research Policy, as PI, it is your responsibility to inform co-investigators, staff, or students involved in the design, conduct, or reporting of externally sponsored research of their requirement to complete a Conflict of Interest in Research Disclosure Form.

X **I accept this responsibility.**

X **The Principal Investigator has read and agrees to the above certifications and will abide by the above obligations.**

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* * * Event History * * *

Event History

Date	Status	View Attachments	Letters
01/13/2020	CONTINUING REVIEW 4 FORM APPROVED	Y	Y

01/08/2020	CONTINUING REVIEW 4 FORM REVIEWER(S) ASSIGNED		
12/10/2019	CONTINUING REVIEW 4 FORM SUBMITTED	Y	
12/03/2019	CONTINUING REVIEW 4 FORM CREATED		
10/21/2019	AMENDMENT 11 FORM APPROVED	Y	Y
10/19/2019	AMENDMENT 11 FORM REVIEWER(S) ASSIGNED		
10/14/2019	AMENDMENT 11 FORM SUBMITTED	Y	
10/14/2019	AMENDMENT 11 FORM CREATED		
01/10/2019	CONTINUING REVIEW 3 FORM APPROVED	Y	Y
01/08/2019	CONTINUING REVIEW 3 FORM REVIEWER(S) ASSIGNED		
01/07/2019	CONTINUING REVIEW 3 FORM PANEL REASSIGNED		
01/04/2019	CONTINUING REVIEW 3 FORM SUBMITTED	Y	
12/20/2018	CONTINUING REVIEW 3 FORM CREATED		
07/24/2018	AMENDMENT 10 FORM APPROVED	Y	Y
07/24/2018	AMENDMENT 10 FORM REVIEWER(S) ASSIGNED		
07/23/2018	AMENDMENT 10 FORM SUBMITTED	Y	
07/23/2018	AMENDMENT 10 FORM CREATED		
05/01/2018	AMENDMENT 9 FORM APPROVED	Y	Y
04/30/2018	AMENDMENT 9 FORM REVIEWER(S) ASSIGNED		
04/23/2018	AMENDMENT 9 FORM SUBMITTED	Y	
01/19/2018	AMENDMENT 9 FORM CREATED		
01/19/2018	CONTINUING REVIEW 2 FORM APPROVED	Y	Y

01/18/2018	CONTINUING REVIEW 2 FORM REVIEWER(S) ASSIGNED		
01/16/2018	CONTINUING REVIEW 2 FORM SUBMITTED (CYCLE 1)	Y	
01/11/2018	CONTINUING REVIEW 2 FORM PANEL MANAGER REVIEW		
01/09/2018	CONTINUING REVIEW 2 FORM SUBMITTED	Y	
12/22/2017	CONTINUING REVIEW 2 FORM CREATED		
08/10/2017	REPORT 2 FORM APPROVED	Y	Y
07/21/2017	REPORT 2 FORM REVIEWER(S) ASSIGNED		
07/20/2017	REPORT 2 FORM PANEL MANAGER REVIEW		
07/14/2017	REPORT 2 FORM PANEL REASSIGNED		
07/07/2017	REPORT 2 FORM REVIEWER(S) ASSIGNED		
07/07/2017	REPORT 2 FORM PANEL MANAGER REVIEW		
07/07/2017	REPORT 2 FORM PANEL REASSIGNED		
07/07/2017	REPORT 2 FORM PANEL REASSIGNED		
07/07/2017	REPORT 2 FORM PANEL MANAGER REVIEW		
06/26/2017	REPORT 2 FORM PANEL REASSIGNED		
06/26/2017	REPORT 3 FORM DELETED		
06/26/2017	REPORT 3 FORM RETURNED		
06/23/2017	REPORT 3 FORM SUBMITTED	Y	
06/23/2017	REPORT 3 FORM CREATED		
06/22/2017	REPORT 2 FORM SUBMITTED	Y	

06/20/2017	REPORT 2 FORM CREATED		
06/13/2017	AMENDMENT 8 FORM APPROVED	Y	Y
06/12/2017	AMENDMENT 8 FORM REVIEWER(S) ASSIGNED		
06/12/2017	AMENDMENT 8 FORM SUBMITTED (CYCLE 1)	Y	
06/08/2017	AMENDMENT 8 FORM PANEL MANAGER REVIEW		
06/08/2017	AMENDMENT 8 FORM SUBMITTED	Y	
06/06/2017	AMENDMENT 8 FORM CREATED		
05/30/2017	AMENDMENT 7 FORM APPROVED	Y	Y
05/26/2017	AMENDMENT 7 FORM REVIEWER(S) ASSIGNED		
05/23/2017	AMENDMENT 7 FORM SUBMITTED	Y	
05/19/2017	AMENDMENT 7 FORM CREATED		
02/08/2017	AMENDMENT 6 FORM APPROVED	Y	Y
02/07/2017	AMENDMENT 6 FORM REVIEWER(S) ASSIGNED		
02/03/2017	AMENDMENT 6 FORM SUBMITTED	Y	
01/31/2017	AMENDMENT 6 FORM CREATED		
12/22/2016	CONTINUING REVIEW 1 FORM APPROVED	Y	Y
12/22/2016	CONTINUING REVIEW 1 FORM REVIEWER(S) ASSIGNED		
12/06/2016	CONTINUING REVIEW 1 FORM SUBMITTED	Y	
11/21/2016	CONTINUING REVIEW 1 FORM CREATED		
09/23/2016	AMENDMENT 5 FORM APPROVED	Y	Y
09/22/2016	AMENDMENT 5 FORM REVIEWER(S) ASSIGNED		

09/20/2016	AMENDMENT 5 FORM SUBMITTED (CYCLE 1)	Y		
09/19/2016	AMENDMENT 5 FORM PANEL MANAGER REVIEW			
09/16/2016	AMENDMENT 5 FORM SUBMITTED	Y		
09/13/2016	AMENDMENT 5 FORM CREATED			
09/12/2016	AMENDMENT 4 FORM APPROVED	Y		Y
09/09/2016	AMENDMENT 4 FORM REVIEWER(S) ASSIGNED			
09/06/2016	AMENDMENT 4 FORM SUBMITTED	Y		
09/06/2016	AMENDMENT 4 FORM CREATED			
05/27/2016	REPORT 1 FORM APPROVED	Y		Y
05/20/2016	REPORT 1 FORM REVIEWER(S) ASSIGNED			
05/19/2016	REPORT 1 FORM SUBMITTED	Y		
05/19/2016	REPORT 1 FORM CREATED			
04/12/2016	AMENDMENT 3 FORM APPROVED	Y		Y
04/12/2016	AMENDMENT 3 FORM REVIEWER(S) ASSIGNED			
04/07/2016	AMENDMENT 3 FORM SUBMITTED	Y		
04/07/2016	AMENDMENT 3 FORM CREATED			
02/24/2016	AMENDMENT 2 FORM DELETED			
02/24/2016	AMENDMENT 2 FORM CREATED			
02/24/2016	AMENDMENT 1 FORM APPROVED	Y		Y
02/23/2016	AMENDMENT 1 FORM REVIEWER(S) ASSIGNED			
02/18/2016	AMENDMENT 1 FORM SUBMITTED	Y		

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02/17/2016	AMENDMENT 1 FORM CREATED		
02/17/2016	NEW FORM APPROVED	Y	Y
02/16/2016	NEW FORM REVIEWER(S) ASSIGNED		
02/09/2016	NEW FORM SUBMITTED (CYCLE 2)	Y	
01/27/2016	NEW FORM SUBMITTED (CYCLE 1)	Y	
01/11/2016	NEW FORM REVIEWER(S) ASSIGNED		
01/04/2016	NEW FORM PANEL ASSIGNED		
12/31/2015	NEW FORM SUBMITTED	Y	
12/28/2015	NEW FORM PREREVIEWED		
12/17/2015	NEW FORM PREAPPROVAL		
08/31/2015	NEW FORM CREATED		