GNFIRB#V12025

June 1, 2025

Title: OVARIAN PLATELET-RICH PLASMA (oPRP) INJECTIONS FOR IMPROVEMENT IN IVF PATIENTS BASED ON TIME-LAPSE INCUBATOR CULTURE FOR AUTOMATED TRACKING AND AI FOR EMBRYO QUALITY ASSESSMENT: A NON-RANDOMIZED PROSPECTIVE SELF-CONTROLLED INTERVENTIONAL STUDY

Sponsor: Generation Next Fertility

Investigators:

Jesse J. Hade MD, Janelle Luk MD, Edward Nejat MD, Serin Seckin MD, Alicia Broussard PhD
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Proposal Voted on and Approved by Committee on 3/24/2025

10.0

Title of Policy: Research & Ethical Advisory Board

Policy Number: GNF0103

Date of Initiation: 01/01/2021

Last Revision/Update: 01/01/2021

Policy Author: Vitaly A. Kushnir, MD

All research at Generation Next Fertility (GNF) is performed under the supervision of Institutional Review Board (IRB), which is to include fair representation of the community, infertility patients, GNF staff and researchers.

The IRB is to be headed by a Chair, who preferably should not be an employee of GNF.

The IRB Chair may appoint a sub-committee to help in the conduct of his/her responsibilities.

IRB meetings are to be called per need and may be held by teleconference.

A current listing of members is Vitaly A. Kushnir, MD, Joshua Johnson, MD, Michael Heard, MD

Because research represents such an integral part of GNF, the initial informed consent documents patients sign upon initial visit to GNF, shall inform them that all medical record and discarded biological specimens at GNF may be utilized for medical research and/or quality control purposes. Moreover, patients shall be informed in these documents that no further consent may be required from them for use of their medical records or discarded biological specimens in research and/or quality control activities, as long as confidentiality is maintained and the identity of patients remains protected.

No research shall be performed on medical records or discarded biological specimens, unless consent, containing such language, was signed by the patient.

A. DEFINITIONS

The IRB represent an oversight body, constituted of GNF employees and external board members, charged with overseeing certain activities at GNF. Activities under IRB oversight, include all activities relating to the performance of assisted reproduction (i.e., in vitro fertilization and related procedures) and all research activities at GNF.

Moreover, the IRB shall serve as GNF's human subject and ethical advisory board, which shall be consulted by GNF staff whenever ethical issues arise, which are not clearly defined by the standard of daily clinical care, practiced at GNF and in the community.

IRB members are subject to annual appointments and re-appointments by the ART Director or designee of GNF.

There shall be no payments made to IRB members, though they may receive reimbursement for expenses incurred in fulfillment of their responsibilities as IRB members.

While IRB members are subject to appointment by the ART Director or designee of GNF, the IRB shall be representative of GNF as well as general community interests. Therefore, the position of Chair shall be filled by an external (non-GNF employed) individual, who shall be either a physician or scientist and, preferably, a majority of board members shall be representative of community interests (i.e., be external board members). The ART Director or designee of GNF shall serve as Vice-Chair of the IRB.

The IRB shall in all of its functions report directly to the Board of Directors of GNF. While the ART Director or designee of GNF appoints IRB members, involuntary dismissal of IRB members shall only be possible by decision of the Board of Directors of GNF.

Since members of the IRB may have access to confidential patient data, they shall be obliged to sign a confidentiality agreement with GNF, which mandates that all patient information they become privy to be held in confidence and not be communicated to any third parties.

B. MISSION STATEMENT:

The mission of GNF's IRB is to assure that all clinical and research activities, conducted at GNF, comply with basic human rights, as defined by the revised Declaration of Helsinki, passed in October 2000 at the 52nd World Medical Association General Assembly in Edinburgh, Scottland, UK and that any form of animal experimentation, if conducted at

GNF, follows internationally accepted guidelines for the protection of animals in such research.

C. PROCESS IMPLEMENTATION:

All application forms, required for submission to the IRB, shall be electronically available from the business offices of GNF.

The IRB shall meet per need, as defined by Chair or Vice-Chair. A quorum is defined as the presence of at least one third of appointed members.

Meetings of the IRB shall follow rules and shall be documented by minutes, to be signed by Chair or Vice-Chair.

Agenda and items, submitted for review to any IRB meeting, shall be distributed to all IRB members at least five (5) working days in advance of such meeting to allow for proper familiarization with materials.

Each research project, submitted for review to the IRB, shall be numbered with date of IRB meeting when first reviewed and consecutive project number of that meeting (i.e., for example 8/21/19-1, denoting the first project reviewed by the IRB on 8/21/19).

The principal investigator (PI) for each research project shall be principally responsible for annual progress and/or completion reports.

GNF's manager shall maintain all IRB files and shall inform Chair of IRB in timely fashion of annual and/or completion reports that become due.

Items submitted for review by the IRB may be of the following nature:

(i) INFORMAL REPORT:

Purpose: Information of IRB members only; no decision expected/required.

Examples: IVF-related outcome reports, or informal updates on previously approved research projects.

(ii) INQUIRY:

Purpose: Question to IRB;

Examples: Ethical concerns or introduction of ethically controversial new clinical technique in IVF.

(iii) NEW RESEARCH PROJECT:

Purpose: Review and approval;

(iv) EXPEDITED REVIEW:

Purpose: Expedited review and approval by Chair alone.

(v) RE-APPROVAL/TERMINATION OF RESEARCH PROJECT

Purpose: Re-approval or termination;

Requests for IRB involvement in regards to (i), (ii) and (v) shall take the format of a formal letter “to the IRB”.

Requests for IRB involvement in regards to (iii) shall take the format of a formal research project review, using standard GNF IRB format (Appendix), including a covering letter by the principal investigator (PI) “to the IRB,” requesting review and approval of the proposed project.

Requests for IRB involvement in regards to (iv) shall take the format of a formal letter from the PI “to the IRB,” requesting expedited review and approval of a project by the Chair. Such a letter shall contain: (1) a description of reason(s) why expedited (in place of full IRB) review appears appropriate (see below); (2) documentation by supporting documents (i.e., prior IRB approvals of project at other institution, etc).

CRITERIA FOR EXPEDITED REVIEW

All research shall be reviewed by the full IRB unless criteria for expedited review of a project are met, in which case only the Chair, under his full discretion, can choose to grant expedited review and approval. The Chair, at own discretion, can at any moment return such expedited review to review by the complete IRB.

In case the Chair grants expedited review and approves a project, he shall issue a formal written approval letter for the project, which shall otherwise administratively be handled like any other research project, reviewed by the IRB, with the date of the decision letter being considered the date of IRB review.

Criteria for expedited review exist if:

(i) A research project has previously undergone detailed review and approval at another formal IRB and such process is documented.

(ii) GNF joins a research project, already elsewhere underway, and at that other institution reviewed and approved by a formal IRB.

(iii) Another institutions wishes to join a GNF project, already previously reviewed and approved by GNF’s IRB.

(iv) The complete IRB has granted the Chair specific authority.

APPENDIX

SUBMISSION PACKAGE, REQUESTING REVIEW
AND CONSIDERATION FOR APPROVAL OF
RESEARCH PROJECT BY GNF’s IRB

[ ] EXPEDITED REVIEW

New Research Project

[x] COMPLETE APPLICATION

RESEARCH SUBJECT OVARIAN PLATELET-RICH PLASMA INJECTIONS AND AI EMBRYO ASSESSMENT INFORMATION & CONSENT FORM

Title: OVARIAN PLATELET-RICH PLASMA (oPRP) INJECTIONS FOR IMPROVEMENT IN IVF PATIENTS BASED ON TIME-LAPSE INCUBATOR CULTURE FOR AUTOMATED TRACKING AND AI FOR EMBRYO QUALITY ASSESSMENT: A NON-RANDOMIZED PROSPECTIVE SELF-CONTROLLED INTERVENTIONAL STUDY

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IVF AND PRP HISTORICAL CONTEXT

In vitro fertilization (IVF) was first successfully employed in a human in 1978 during an unstimulated natural cycle, leading to the birth of Louise Brown, the first IVF baby. Due to the limited success of natural IVF cycles, gonadotropins were introduced as a means to stimulate the growth and maturation of multiple antral follicles before oocyte retrieval, significantly improving the efficiency of IVF treatments. Over the years, controlled ovarian stimulation has enhanced the success of IVF by increasing the number of mature oocytes retrieved, thereby improving fertilization rates and the likelihood of achieving pregnancy and live birth.

Autologous platelet-rich plasma (PRP) was introduced as a transfusion product by hematologists in the 1970s for the treatment of thrombocytopenia. PRP is defined as plasma with a platelet concentration above that of peripheral blood and has since been widely adopted in various medical fields, including orthopedics, cardiothoracic surgery, plastic surgery, dermatology, dentistry, and diabetic wound healing, due to its regenerative properties.

The first recorded ovarian PRP (oPRP) procedure was performed in 2018, demonstrating improvements in ovarian function, folliculogenesis, and ovulation induction, particularly in patients with diminished ovarian reserve. Preliminary studies have suggested that oPRP injections may enhance ovarian reserve markers, increase the number of retrieved mature oocytes, and improve embryo quality, leading to better IVF outcomes. The mechanism behind oPRP's efficacy is believed to involve growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which contribute to tissue regeneration and angiogenesis within the ovarian microenvironment.

The potential benefits of PRP for ovarian and endometrial rejuvenation have been postulated based on data extrapolated from prior medical research. However, despite promising initial findings, most of the information demonstrating the benefit of PRP on ovarian reserve, oocyte quality, and embryo development remains limited to anecdotal evidence and small-scale studies. Large-scale, well-controlled clinical trials are needed to establish definitive efficacy and safety in this domain.

PURPOSE OF THIS RESEARCH

This is a non-randomized prospective self-controlled interventional study evaluating the impact of oPRP injections on embryo quality in patients undergoing two IVF cycles.

Participants will undergo two IVF cycles at Generation Next Fertility.

The first cycle will serve as the control (no oPRP treatment), while the second study cycle will incorporate oPRP injections.

Oocytes retrieved will undergo fertilization using one of the following methods:

Conventional Insemination

Intracytoplasmic sperm injection (ICSI)

ICSI with Zymot

ICSI with Zymot and Physiological ICSI (PICSI)

Patients may opt for Preimplantation Genetic Testing for Aneuploidy (PGT-A) through Genomic Prediction LLC's LifeView™ platform, which utilizes single nucleotide polymorphism (SNP) technology to enhance accuracy in detecting chromosomal abnormalities.

All embryos from both IVF cycles will be cultured in a time-lapse incubators for automated tracking and assessment.

Embryo quality will be measured by an AI software used in conjunction with the time-lapse incubators.

This study aims to evaluate whether ovarian platelet-rich plasma (oPRP) injections improve embryo quality in In Vitro Fertilization (IVF) cycles. Patients will undergo two IVF cycles:

First cycle (Control cycle): A standard IVF cycle with individualized ovarian stimulation protocols based on AMH, AFC and patient history and prior IVF outcomes when applicable.

Second cycle (Study cycle): Includes oPRP injections, administered:

1-2 weeks after the onset of menses following the first IVF cycle.

A second injection between stimulation days 2-5 of the second IVF cycle.

The protocol of the second IVF cycle will be again based on the same criteria as the first IVF cycle. Embryos from both cycles will be monitored using a time-lapse incubator in conjunction with an AI software to analyze embryo development and assess Embryo Quality (EQ) scores. The study will determine if oPRP improves embryo quality and implantation potential. Each embryo will be given an EQ (embryo quality) score based on the morphokinetics of the embryos during the incubation period. The Embryo Quality (EQ) Score, generated through AI analysis, will be used to assess whether oPRP improves embryo development, viability, and implantation potential. No clinical decision will be made based upon the resulting Embryo Quality (EQ) Score. The time-lapse based AI software for embryo assessment is an investigational device, which means that it is not approved by the Food and Drug Administration (FDA)

STUDY PROTOCOL

1. Baseline Evaluation & Enrollment

All participants will undergo a baseline ultrasound and hormonal blood workup at the start of their menstrual cycle, approximately one month or more prior to initiating the first IVF cycle. This baseline assessment will include:

Ultrasound to determine antral follicle count (AFC) and assess ovarian morphology.

Hormonal testing including Anti-Müllerian Hormone (AMH), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), Progesterone (P4), Thyroid Stimulating Hormone (TSH), Prolactin (PRL) and Beta-Human Chorionic Gonadotropin (β-hCG).

Routine infectious disease screening in compliance with IVF laboratory standards for both the patient and any male partner.

Genetic Carrier screening through Horizon™ advanced carrier screening test by Natera, Inc. will be offered to all patient’s and their partners

Semen Analysis for all male partners to determine if a male factor infertility is present.

Patients will then proceed with their first IVF cycle under a standardized ovarian

stimulation protocol based on their ovarian reserve and history of previous IVF response when applicable.

2. First IVF Cycle (Control)

The first IVF cycle will serve as a control cycle, conducted without oPRP injections.

The ovarian stimulation protocol (natural, mild, or conventional) will be determined based on AFC and hormonal profile.

Once the lead follicle reaches the appropriate size (≥18 mm), ovulation will be induced using 10,000 IU of human chorionic gonadotropin (hCG) or 250 mcg Ovidrel®, or 80-100 IU of Leuprolide acetate or a combination of the above administered approximately 35.5 hours prior to retrieval.

Oocyte retrieval will be performed under deep intravenous (IV) sedation by a board-certified anesthesiologist, using transvaginal ultrasound guidance.

Fertilization Method Options:

Conventional Insemination

Intracytoplasmic sperm injection (ICSI)

ICSI + Zymot sperm selection

ICSI + Zymot + Physiological ICSI (PICSI)

With or without PGT-A using SNP-based LifeView® technology from Genomic Prediction LLC.

Up to 15 embryos will be cultured in the time-lapse incubator, which in conjunction with AI, provides an automated embryo quality score based on morphokinetic parameters. The resulting AI Score will not be used to guide any clinical decisions.

All embryos reaching the blastocyst stage will be biopsied (if PGT-A is elected), vitrified, and stored for potential future embryo transfer.

3. oPRP Treatment & Second IVF Cycle (Study Cycle)

Following the first IVF cycle, patients will undergo their first oPRP injection:

Timing: 1-2 weeks after the onset of the next menstrual cycle.

Procedure: Under IV sedation, a patient’s autologous PRP will be prepared and injected directly into both ovaries under transvaginal ultrasound guidance.

Second IVF Cycle (oPRP Study Cycle)

The same ovarian stimulation protocol will be used for consistency.

A second oPRP injection will be performed on stimulation days 2-5 to enhance folliculogenesis.

Ovulation will be triggered at the same follicular size thresholds, and oocyte retrieval will follow identical protocols.

Fertilization methodology will be identical to the first cycle unless no fertilization is identified in the first cycle.

Embryo Development Analysis: Up to 15 embryos will be cultured in a time-lapse incubator, which in conjunction with AI, provides an automated embryo quality score based on morphokinetic parameters. The resulting AI Score will not be used to guide any clinical decisions.

4. Data Collection & Outcome Measures

Primary vs. Secondary Outcome Measures

Primary Outcome Measure:

Improvement in blastocyst formation rate following oPRP treatments, as assessed by the use of a time-lapse incubator in conjunction with AI.

Secondary Outcome Measures:

Improvement in embryo quality based on Morphokinetics using the AI score from time-lapse videography.

Changes in ovarian reserve markers (AMH, AFC, FSH, E2) post-oPRP.

Increase in the number of mature (MII) oocytes retrieved in the second IVF cycle.

Increase in 2 PN embryos formed

Increase in Day 3 embryos formed with 6 cells or more

Increase in Blastocysts formed

Increase in High Quality blastocysts formed (3BB or better)

Increase in Euploid embryos based on PGT-A analysis when available

Clinical pregnancy rate per embryo transfer.

Live birth rate following embryo transfer.

MONITORING & SAFETY

Patients will be closely monitored throughout both IVF cycles to ensure optimal response and minimize risks.

Bloodwork and ultrasound assessments will be conducted regularly to track follicular development, endometrial thickness, and hormonal response.

Any adverse events, including ovarian hyperstimulation syndrome (OHSS), infection, or complications related to IVF or oPRP injections, will be documented and reported.

Safety data from over 940 oPRP injections performed to date at GNF since July 2021 indicate no major complications requiring hospitalization, blood or blood product transfusion, surgery, or other interventional procedures.

The most commonly reported side effect from the ovarian PRP procedure was transient pain at the ovarian injection site, lasting a maximum of four days, all of which resolved with expectant management.

Inclusion & Exclusion Criteria

Inclusion Criteria:

Patients age 18 to 47 who are eligible for both In Vitro Fertilization (IVF) and ovarian Platelet-Rich Plasma (oPRP) injections.

No known contraindications to IVF or oPRP as outlined in the exclusion criteria.

Willing to undergo two consecutive IVF cycles, with the first cycle serving as a control and the second cycle including oPRP injections.

Adequate ovarian reserve based on baseline antral follicle count (AFC) and anti-Müllerian hormone (AMH) levels.

Exclusion Criteria:

Patients will be excluded from participation if they meet any of the following conditions:

Anovulation due to perimenopause or menopause, as determined by clinical evaluation and laboratory testing

Ovarian accessibility issues, including:

Ovaries not accessible via transvaginal ultrasound
Large unresolved ovarian cysts
History of ovarian abscess or pelvic infection
Any medical condition where pregnancy is contraindicated, including but not limited to:
Severe cardiovascular disease
Uncontrolled hypertension or diabetes
Renal or hepatic insufficiency
History of malignancies, including:
Breast, gynecologic, hematologic (leukemia, lymphoma), or other cancers
Borderline ovarian tumors
Hematologic disorders, including:
Anemia (low hemoglobin/hematocrit levels)
Sickle cell disease, beta-thalassemia, or alpha-thalassemia
Polycythemia (abnormal increase in red blood cells)
Thrombocytopenia (low platelet count) or any platelet dysfunction disorder
Hypercoagulable conditions, such as:
Deep vein thrombosis (DVT)
Pulmonary embolism (PE)
History of stroke or transient ischemic attack (TIA)
Uncontrolled or poorly managed autoimmune diseases, including:
Systemic lupus erythematosus (SLE)
Sjögren’s syndrome
Uncontrolled diabetes mellitus
Severe uncontrolled thyroid dysfunction (hypothyroidism or hyperthyroidism)
Use of medications contraindicated for IVF or oPRP, including:
NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)
Anticoagulants or blood thinners (oral or injectable, e.g., Lovenox, Heparin, Warfarin)
Chronic corticosteroid use
Substance use that may negatively impact IVF or oPRP response, including:
Excessive alcohol consumption
Recreational drug use
Prior oPRP treatment within the past 6 months
Patients unwilling or unable to complete two consecutive IVF cycles
Patients under the age of 18 or over the age 47

NUMBER OF SUBJECTS / LENGTH OF PARTICIPATION

This study employs a prospective non-randomized self-controlled design, where each patient serves as their own control by undergoing two IVF cycles—one without oPRP (control cycle) and one following two oPRP treatments (study cycle). While this design reduces inter-patient variability, we acknowledge the potential for time-dependent confounders and variations in ovarian response.

Baseline Blastocyst Formation Rate per Oocyte Retrieved: 25% (based on retrospective

clinical data).

Expected Improvement of Blastocyst formation rate with oPRP: 35% (a 10% absolute increase, representing a 40% relative improvement).

Statistical Parameters:

Power: 80%

Alpha (Significance Level): 0.05

Study Design: Self-controlled (paired analysis)

Based on these parameters, we aim to detect a minimum detectable effect size of approximately a 10% absolute increase in blastocyst formation rate (from 25% to 35%). To achieve this, a total sample size of 180 patients is required. This calculation accounts for the paired nature of the study design and the expected discordant proportions between the control and study cycles.

To maintain statistical robustness, we have chosen a sample size of 180 patients, which includes an estimated 10-15% dropout rate for cycle cancellations or variability in ovarian response. An interim analysis will be conducted at 50% enrollment to validate initial assumptions regarding oPRP's impact on blastocyst formation.

This study will also consider an external control group of patients undergoing two IVF cycles without oPRP to further validate findings and minimize bias.

BENEFITS

Participation in this study may offer personal reproductive benefits, as the use of ovarian platelet-rich plasma (oPRP) injections has been associated with enhanced ovarian function, improved folliculogenesis, and increased oocyte quality in preliminary studies. These improvements may, in turn, increase the number of mature oocytes retrieved, improve embryo development, and enhance implantation potential, potentially improving the likelihood of pregnancy.

A key component of this study is the use of a time-lapse incubator in conjunction with AI, which will provide real-time, continuous monitoring of embryo development. This advanced imaging technology allows for detailed morphokinetic analysis of embryos. By using this cutting-edge incubator, we aim to further optimize embryo selection, reduce subjectivity in grading, and potentially improve IVF outcomes.

While these potential benefits exist, it is important to acknowledge that pregnancy cannot be guaranteed, and some or all participants may not experience any improvement in their fertility outcomes. However, if oPRP proves to be beneficial, this research may have far-reaching implications for reproductive medicine, offering an innovative and less invasive alternative for women with poor ovarian response or diminished ovarian function.

Additionally, this study may contribute to advancing fertility treatments, helping future patients by providing more data on the efficacy of oPRP in IVF and refining embryo quality assessment using AI-driven technology. By participating, you will be contributing to cutting-edge reproductive research that could enhance success rates and reduce the overall burden of fertility treatments in the future.

Compensation for Participation

The primary goal of this study is to assess the potential benefits of ovarian platelet-rich

plasma (oPRP) injections in improving IVF outcomes. Participants in this study will receive a substantial reduction in the cost of specific services provided by Generation Next Fertility (GNF), including:

Two discounted IVF cycles, inclusive of ovarian follicular monitoring and oocyte retrieval for patient's not using their health insurance coverage for this treatment.

Two free oPRP injections (both the initial and second treatment)

Free Intracytoplasmic Sperm Injection (ICSI)

Discounted Zymot and PICSI sperm selection methods (if chosen)

Discounted Embryo biopsy fee for Preimplantation Genetic Testing for Aneuploidy, monogenetic diseases or structural rearangements (PGT-A/M/SR) (if chosen)

Free embryo cryopreservation and storage for up to 6 months

Free use of the time-lapse incubator with AI for continuous embryo monitoring and evaluation

Sources of Funding

This research study is fully funded by Generation Next Fertility, PLLC. No external funding sources or third-party financial sponsorships are involved.

Patient Financial Responsibility

Patients will be responsible for:

The full cost of PGT-A/M/SR tissue analysis if they choose to proceed with genetic testing of their embryos

Any additional embryo storage fees beyond the six-month complimentary period

All medical expenses related to pregnancy beyond the first pregnancy test

Any non-study-related procedures or treatments

The full cost of ovarian stimulation medications required for both IVF cycles

The full cost of the frozen embryo transfer (FET) cycle if an embryo is cryopreserved

Insurance Coverage Considerations

Patients using insurance coverage for IVF treatments at Generation Next Fertility will receive a discount on all out-of-pocket expenses for procedures not covered by insurance. However, this discount does not apply to medication costs, PGT-A/M/SR embryo analysis, anesthesia-related services, or the FET cycle, which remain the patient's financial responsibility.

Important Considerations

No monetary compensation will be provided for participation in this study.

Participation in the study does not guarantee pregnancy or improved fertility outcomes.

The cost reduction only applies to services rendered by Generation Next Fertility and does not cover external laboratory fees, additional medical costs, medications, prolonged embryo storage fees beyond 6 months, or the cost of the frozen embryo transfer cycle.

SUBMISSION CHECK LIST FOR COMPLETE APPLICATIONS

_____ Only complete applications submitted at least 5 business days before an IRB meeting will be considered.

_____ Submit application electronically to IRB Chair

_____ Date of submission is: _____

_____ Application complete; The following was addressed:

I. General Aspects

II. Study Design

III. Informed Consent Information

IV. Project Summary

V. Funding

VI. Principal Investigator Assurance

Appendix

INSTITUTIONAL REVIEW BOARD OF THE GNF CENTER FOR ADVANCED FERTILITY

APPLICATION TO CONDUCT A RESEARCH PROJECT

I. GENERAL ASPECTS: This COMPLETE application for review by the IRB of GNF applies only to projects initiated at GNF or in collaboration with GNF. Projects initially initiated at other medical institutions, which GNF staff wishes to join in a collaborative effort, shall be first reviewed and approved by an outside IRB, responsible for project reviews at the originating medical institution. Once approval of the project has been obtained by that IRB, an EXPEDITED REVIEW by the Chair of the GNF IRB can be requested. In case such an expedited review is requested, only Section I of this application (General Aspects) is to be completed and all relevant materials from the other institution's IRB review and approval are to be attached.

This is a request for a [x] COMPLETE REVIEW [ ] EXPEDITED REVIEW

Title of Proposal: RESEARCH SUBJECT OVARIAN PLATELET-RICH PLASMA AND TIME-LAPSE INCUBATOR WITH AI INFORMATION & CONSENT FORM

Principal Investigator: Jesse Hade, MD

The Principal Investigator (PI) is the principally responsible individual to the IRB for submission of a complete application and the content as well as veracity of this application. He/she is also the principally responsible individual for the proper conduct of any IRB-approved research project.

Co-Investigators: Janelle Luk, MD, Edward Nejat, MD, Serin Seckin, MD, Alicia Broussard, PhD

Performance Site(s): Generation Next Fertility

Funded by:

[ ] Intramural funds

[x] Other: Generation Next Fertility

Requested time period for approval of project: 60 days

In submitting this project, I declare that:

[x] None of the investigators has any conflict to declare that in any form

whatsoever may be relevant to conduct of this research project.

[ ] The following potential conflicts exist: _____ 7

_____

All potential significant conflicts, involving all investigators, shall be listed. This means that every

significant financial interest that reasonably would appear to be affected by the research activity or

interest in entities whose financial interests would reasonably appear to be affected by the research

activity. Conflicts also include family interests of spouses and children. Use additional page, if

required.

II. STUDY DESIGN:

Human Subjects: YES [x] NO [ ]

If YES, describe in detail in section below how human subjects will be involved. Specifically

indicate if only human materials and/or human medical records are involved in the study and

no experimentation, involving patients directly, is proposed. If research does not involve intact

human, indicate how material(s) will be obtained (i.e., pathologic discards, surgical specimens,

donations of body fluids, etc). You also have to indicate number of patients expected to be investigated, whether they will be adults or minors and age ranges. If medical records are used , describe any potential psychological and sociological risk to patients (if any) and note in application that all GNF patients at time of first consultation sign informed consents, which allows for the review of their medical records as long as their identities remain undisclosed in the process and medical records remain confidential. Indicate in your application how these conditions will be met. Also indicate whether study involves randomization, placebo use and describe each study group in detail. Indicate whether study subjects receive a fee to participate or any other inducement (s). Use additional page if required.

Experimental Drugs (new drug usage or dosage): YES [ ] NO [x]

Experimental Device: YES [X] NO [ ]

If YES for either one, describe in detail how human subjects will be involved.

The AI software, an investigational device in the US, is based on convolutional neural networks (CNN) and is intended as a support tool designed to evaluate early embryo development using time-lapse videos. It provides automatic annotations of human embryos and predicts embryo viability. The software is intended for use by professional embryologists, laboratory personnel, and clinical staff at IVF clinics. The AI software may be considered a non-significant risk (NSR) device, as it does not direct patient management, alter clinical decisions, or interfere with the standard of care. Its output is for observational and investigational purposes only. In the context of this protocol, subjects and embryos do not directly benefit from the investigational AI device, as the

protocol does not affect the standard of care or treatment. The AI outcome may be shared with participants, the research outcomes may facilitate an improvement in IVF patient care, which may potentially benefit the subject.

Informed Consent:

Does study involve obtaining a full informed consent? YES [x] NO [ ]

If YES, attach copy of full written informed consent proposed for this study. If no consent is to be obtained, attach written justification why no consent is obtained. Indicate whether a STANDARD or ABBREVIATED informed consent form will be used. Standard consents must contain all required elements for informed consent. Abbreviated consents (a short one-page consent) shall be used only in studies which only involve blood donations from healthy subjects in amounts not exceeding 450ml in one 8-week period and not more often than twice weekly.

Further details on the requirements of full informed consent are listed below in Section III (Informed Consent Information)

Criteria why no consent may be obtained are:

(i) Research involves no more than minimal risk to research subjects, with minimal risk being defined by IRB policy, based on internationally practiced criteria.

(ii) Omitting a consent will not adversely affect rights and welfare of study subjects.

(iii) The research could not practically carried out without a waiver of consent.

(iv) Whenever appropriate, study subjects will receive additional pertinent information after participation.

Recruitment of Study Subjects:

Does study recruitment involve advertisement? YES [x] NO [ ]

If YES, attach copy of proposed advertisement for prior approval by IRB.

Agreement of Human Subjects: As PI I agree to bring any proposed significant changes in this research project or in its activities, that may affect human subjects, immediately to the attention of the IRB for its approval. I also agree to bring any emerging problems for review and recommendations to the attention of the IRB.

JH

_____

Initials

III. INFORMED CONSENT INFORMATION

The following information and phrases (here listed under “____ “) must be contained in a STANDARD informed consent:

(i) PROTECTED HEALTH INFORMATION:

“All information in regards to your health is personal and GNF is obliged to protect the privacy of that information. We herby remind you that, upon becoming a GNF patient, you gave us in writing permission to disclose your protected health information for research purposes, as long as such disclosure does not reveal your identity and or breach the confidentiality of that information. We here want to make certain that you are properly informed how this information will be used in research and/or disclosed, assuring continuous confidentiality.

By signing this consent form you reaffirm your permission. You, however, have no obligation to sign this reaffirmation and such refusal will in no way affect your clinical care at GNF.”

“All medical information in your medical record at GNF may be subject to review as part of this study. This means that members research team at GNF, conducting this study, may have access to your protected health information, even if they have not been part of the clinical team, providing medical care to you at GNF. Your information may also be reviewed by members of the Institutional Review Board (IRB) of GNF, which is a community board, charged with assuring that all research at GNF is conducted in accordance with generally accepted rules that protect human rights of research participants. Your information may also be

shared with potential sponsors of research, conducted at GNF, and their agents, the U.S. Food and Drug Administration (FDA) and/or the U.S. Office for Human Research Protection of the U.S. Department of Health and Human Services. Finally, your data may also be shared with colleagues at other medical centers, participating and/or collaborating in GNF’s research.”

“Your health information will be kept for at least 10 years, but possibly indefinitely, and your authorization, therefore, does not expire. You, however, can cancel your authorization at any time, though already authorized and used data cannot be withdrawn.”

“You may ask to see your health information used for this study, but you may have to wait until the end of the study since many study protocols do not allow interim analysis of study data.”

“While we make every possible effort to maintain confidentiality of your medical information and of your identity, we cannot offer an absolute guarantee that we will be successful. While all individuals, given access to this information during the study normally protect the privacy of your medical information, they may not be required to do so by law.”

“Once you sign, you will be given a copy of this informed consent.”

(ii) LANGUAGE RECOMMENDATIONS:

Use “you are being asked to ……” rather than “ I agree to participate in ….”

Make the consent form “user friendly:” Use lay language; Avoid complicated and long sentences; Avoid statements that could be perceived as coercive.

(iii) 8 REQUIRED ELEMENTS:

(1) Purpose of study

(2) Risks and discomforts

(3) Benefits (if any)
(4) Alternatives to participation
(5) Confidentiality [see (i)]
(6) Research-related injury: Must include statement as to whether any compensation and/or medical treatments are available if injury occurs and, if so, provide details. Also detail who should be contacted, and how, in case of injury.
(7) Offer to answer questions: Must include who will be available to do so.
(8) Stress the voluntary nature of all participation [see (i)]. 10
(iv) RECOMMENDED ADDITIONAL ELEMENTS (where appropriate):
(1) A statement that potential risks to patients and offspring (embryo or fetus) may currently be unforeseeable.
(2) A statement that describes circumstances under which a subject's participation in the study may be terminated by investigators without regard to the subject's concerns.
(3) A statement that describes additional costs for the subject (if any) that may result from participation in the research study. Example: "Your participation in this study should not result in costs other than those associated with treatment of your medical condition. The study sponsor will supply study drugs and cover treatment costs at no cost to you." Or: "Some tests and procedures, which are part of your regular care, will not be paid by the study sponsor. Your insurance carrier will be charged for the costs of that care. Some insurance carriers, however, limit what they will pay for routine services, if conducted as part of a research study. In such a case you may be responsible for such costs."
(4) A statement that describes the consequences of a study subject's decision to withdraw from the research, and procedures for orderly termination of participation.
(5) A statement that significant new findings, developed during the course of the research, which may relate to the subjects' willingness to participate, will be provided.
(6) A statement as to the approximate anticipated number of subjects involved in the study.

IV. PRINCIPAL INVESTIGATOR (PI) ASSURANCE
AS PI, I CERTIFY THAT THE INFORMATION SUBMITTED WITHIN THE ACCOMPANYING APPLICATION IS, TO THE BEST OF MY KNOWLEDGE, TRUE, COMPLETE AND ACCURATE. I AM AWARE THAT ANY FALSE, FICTITIOUS OR FRAUDULENT STATEMENTS OR CLAIMS MAY SUBJECT ME TO CRIMINAL, CIVIL OR ADMINISTRATIVE PENALTIES. I AGREE TO ACCEPT RESPONSIBILITY FOR THE SCIENTIFIC CONDUCT OF THE PROJECT AND TO PROVIDE

THE REQUIRED PROGRESS REPORTS IF THIS PROJECT IS APPROVED BY GNF’s IRB AS A RESULT OF THIS APPLICATION.