1. Purpose

1.1. This WI outlines the process by which, SPR Therapeutics will comply with its Financial Conflict of Interest Policy for applicable clinical studies in which Public Health Service (PHS) funding is obtained.

2. Scope

2.1. This WI will apply to all PHS funded clinical studies conducted worldwide; excluding clinical studies funded by SBIR Program Phase I applications.

3. Definitions

3.1 "Disclosure of Significant Financial Interest" means an Investigator's disclosure of Significant Financial Interest (SFI) to an Institution.

3.2 "Financial Conflict of Interest," or "FCOI," means a Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

3.3 "FCOI Report" means an Institution's report of a financial conflict of interest to a PHS Awarding Component.

3.4 "Financial Interest" means anything of monetary value, whether or not the value is readily ascertainable.

3.5 "HHS" means the United States Department of Health and Human Services, and any components of the Department to which the authority involved may be delegated.

3.6 "Institution" means any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that is applying for, or that receives, PHS research funding. SPR Therapeutics is considered an "Institution" for purposes of this policy.

3.7 "Institutional Responsibilities" means an Investigator's professional responsibilities on behalf of SPR Therapeutics, and as defined by SPR Therapeutics in its policy on financial conflicts of interest, which may include for example: activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Data and Safety Monitoring Boards

3.8 "Investigator" means the Project Director or Principle Investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants.

3.9 "Manage" means taking action to address a financial conflict of interest, which can include reducing or eliminating the financial conflict of interest, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

3.10 "PD/PI" means a Project Director or Principle Investigator of a PHS-funded research project; the PD/PI is included in the definitions of senior/key personnel and Investigator under this part.

3.11 "PHS" means the Public Health Service of the U.S. Department of Health and Human Services, and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health (NIH).

3.12 "PHS Awarding Component" means the organizational unit of the PHS that funds the research that is subject to this part.

3.13 "Research" means a systematic investigation, study or experiment designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research. The term encompasses basic and applied research (e.g., a published article, book or book chapter) and product development (e.g., a diagnostic test or drug). As used in this part, the term includes any such activity for which research funding is available from a PHS Awarding Component through a grant or cooperative agreement, whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

3.14 "Senior/Key Personnel" means the PD/PI and any other person identified as a senior/key personnel by SPR Therapeutics in the grant application, progress report, or any other report submitted to the PHS by SPR Therapeutics under this part.

3.15 "Significant Financial Interest" (SFI) means:

3.15.1 A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse or dependent children) that reasonably appears to be related to the Investigator's responsibilities on behalf of SPR Therapeutics:

3.15.1.1 With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. For purposes of this definition, remuneration includes salary, compensation, and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

3.15.1.2 With regard to any non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or

3.15.1.3 Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

3.15.2 Investigators also must disclose the occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their Institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. SPR Therapeutics' FCOI policy for PHS funded study will specify the details of this disclosure, which will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with SPR Therapeutics' FCOI policy, the clinical department head or designee will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes a FCOI with the PHS-funded research.

3.15.3 The term Significant Financial Interest does not include the following types of financial interests: salary, royalties, or other remuneration paid by SPR Therapeutics to the Investigator if the Investigator is currently employed or otherwise appointed by SPR Therapeutics, including intellectual property rights assigned to SPR Therapeutics and agreements to share in royalties related to such rights; any ownership interest in SPR Therapeutics held by the Investigator; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

3.16 "Small Business Innovation Research" (SBIR) Program means the extramural research program for small businesses that is established by the Awarding Components of the Public Health Service and certain other Federal agencies under Public Law 97-219, the Small Business Innovation Development Act, as amended. For purposes of this part, the term SBIR Program also includes the Small Business Technology Transfer (STTR) Program, which was established by Public Law 102-564.

4. Responsibilities

The Clinical Department head, or their designee, will be responsible for the management of Financial Conflict of Interest for PHS Funded Research (and any associated determination of Financial Conflict of Interest from a reported Significant Financial Interest) as described under Section 5.1 specifically pertaining to the Institutional Official and throughout this procedure.

Clinical Department personnel are responsible for collecting information described in this procedure from Investigators or Key Personnel in compliance with this policy and making the Clinical Department head aware of any reported Significant Financial Interest.

5. Procedure

5.1. SPR Therapeutics' (the "Institution") Responsibilities Regarding FCOI to be managed by the clinical department head. The department head, or their designee, will serve as the Institutional Official (IO) for the purposes of this policy.

5.1.1. SPR Therapeutics will maintain an up to date written and enforced FCOI policy that complies with NIH's policies and make such policy available via a publicly accessible Web site. SPR Therapeutics will adhere to this policy and shall provide FCOI Reports regarding identified financial conflicts of interest to the PHS Awarding Component. Individuals with FCOI will not be published on the SPR Website, but this information will be made available within 5 calendar days of a written request by a member of the public.

5.1.2. SPR Therapeutics will inform each investigator partaking in PHS funded research of their FCOI Policy and will inform the investigators of their responsibilities regarding disclosure of significant financial interests, and of NIH's regulations and require each Investigator to complete training regarding the same prior to engaging in research related to any PHS-funded research and at least every four years, and immediately when any of the following circumstances apply:

5.1.2.1. SPR Therapeutics revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Investigators;

5.1.2.2. An Investigator is new to SPR Therapeutics; or

5.1.2.3. SPR Therapeutics finds that an Investigator is not in compliance with SPR Therapeutics' financial conflict of interest policy or management plan.

5.1.3. Prior to SPR Therapeutics' expenditure of any funds under a PHS-funded research project, SPR Therapeutics' will obtain each investigator's disclosure of financial conflict of interest per SPR-SOP-7.2.2 and SPR-FRM-7.2.2ac no later than time of application for the PHS funded research and annually thereafter or when a change occurs. If the investigator discovers or acquires a new Significant Financial Interest the investigator is required to submit an additional disclosure (SPR-FRM-7.2.2ac) within 30 days of discovery or acquisition.

5.1.4. SPR Therapeutics' accounting department will track any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their Institutional responsibilities. At a minimum the purpose of the trip, identity of sponsor/organizers, destination, and duration will be tracked. The accounting department will inform the clinical department head or designee of any Significant Financial Interest an Investigator may have due to travel reimbursement.

5.1.5. Within 60 days of obtaining the investigator financial disclosure, the clinical department head or designee will determine if the investigator has a financial conflict of interest or that the monetary value of travel constitutes as a financial conflict of interest. The clinical department head or designee will then determine whether it is related to PHS-funded research; and, if so, implement, on at least an interim basis, the management plan, outlined below, to specify the actions that have been, and will be, taken to manage such financial conflict of interest. Depending on the nature of the significant financial interest, SPR Therapeutics may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of SPR Therapeutics' review. The management plan may include any of the following.

5.1.5.1. Public disclosure of financial conflicts of interest (e.g., when presenting or publishing the research);

5.1.5.2. For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants;

5.1.5.3. Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias resulting from the financial conflict of interest;

5.1.5.4. Modification of the research plan;

5.1.5.5. Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;

5.1.5.6. Reduction or elimination of the financial interest (e.g., sale of an equity interest); or

5.1.5.7. Severance of relationships that create financial conflicts.

5.1.6. SPR Therapeutics will provide initial and ongoing FCOI Reports to the PHS as required pursuant to SPR-FRM-7.2.2ac

5.1.7. Whenever SPR Therapeutics identifies a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by SPR Therapeutics during an ongoing PHS-funded research project (e.g., was not timely reviewed or reported by a subrecipient), the clinical department head or designee shall, within sixty days: review the significant financial interest; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so:

5.1.7.1. Implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest going forward;

5.1.7.2. In addition, whenever a financial conflict of interest is not identified or managed in a timely manner including failure by the Investigator to disclose a significant financial interest that is determined by SPR Therapeutics to constitute a financial conflict of interest; failure by SPR Therapeutics to review or manage such a financial conflict of interest; or failure by the Investigator to comply with a financial conflict of interest management plan SPR Therapeutics shall, within 120 days of their determination of noncompliance, complete a retrospective review of the Investigator's activities and the PHS-funded research project to determine whether any PHS-funded research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

5.1.7.3. SPR Therapeutics is required to document the retrospective review; such documentation shall include, but not necessarily be limited to, all of the following key elements:

5.1.7.3.1. Project number;

5.1.7.3.2. Project title;

5.1.7.3.3. PD/PI or contact PD/PI if a multiple PD/PI model is used;

5.1.7.3.4. Name of the Investigator with the FCOI;

5.1.7.3.5. Name of the entity with which the Investigator has a financial conflict of interest;

5.1.7.3.6. Reason(s) for the retrospective review;

5.1.7.3.7. Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed);

5.1.7.3.8. Finding of the review; and

5.1.7.3.9. Conclusions of the review.

5.1.7.4. Based on the results of the retrospective review, if appropriate, SPR Therapeutics shall update the previously submitted FCOI Report, specifying the actions that will be taken to

manage the financial conflict of interest going forward. If bias is found, SPR Therapeutics is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component. The mitigation report must include, at a minimum, the key elements documented in the retrospective review above and a description of the impact of the bias on the research project and SPR Therapeutics' plan of action or actions taken to eliminate or mitigate the effect of the bias (e.g., impact on the research project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the research project is salvageable). Thereafter, SPR Therapeutics will submit FCOI reports annually. Depending on the nature of the financial conflict of interest, SPR Therapeutics may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date that the financial conflict of interest or the Investigator's noncompliance is determined and the completion of SPR Therapeutics retrospective review.

5.1.8. Whenever SPR Therapeutics implements a management plan pursuant to this part, SPR Therapeutics shall monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project.

5.1.9. SPR Therapeutics shall provide a written response to any requestor within five business days of a request of information concerning any significant financial interest disclosed to SPR Therapeutics that meets the following three criteria.

5.1.9.1. The significant financial interest was disclosed and is still held by the senior/key personnel as defined by this part;

5.1.9.2. SPR Therapeutics determines that the significant financial interest is related to the PHS-funded research; and

5.1.9.3. SPR Therapeutics determines that the significant financial interest is a financial conflict of interest.

5.1.10. The information that SPR Therapeutics makes available via a written response to any requestor within five business days of a request, shall include, at a minimum, the following:

5.1.10.1. the Investigator's name; the Investigator's title and role with respect to the research project;

5.1.10.2. the name of the entity in which the significant financial interest is held;

5.1.10.3. the nature of the significant financial interest; and the approximate dollar value of the significant financial interest (dollar ranges are permissible: $0-$4,999; $5,000-$9,999; $10,000-$19,999; amounts between $20,000-$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or

5.1.10.4. a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value.

5.1.10.5. SPR Therapeutics' accounting department will be ultimately responsible for keeping these records and provide the information upon request.

5.1.11. SPR Therapeutics will note in its written response that the information provided is current as of the date of the correspondence and is subject to updates, on at least an annual basis and within 60 days of SPR Therapeutics' identification of a new financial conflict of interest, which should be requested subsequently by the requestor.

5.1.12. Information concerning the significant financial interest of an individual shall remain available for responses to written requests for at least three years from the date that the information was most recently updated.

5.2. Reporting of Financial Conflict of Interest Requirements.

5.2.1. Prior to SPR Therapeutics' expenditure of any funds under a PHS-funded research project, SPR Therapeutics shall provide to the PHS Awarding Component an FCOI report regarding any Investigator's significant financial interest found by SPR Therapeutics to be conflicting and ensure that SPR Therapeutics has implemented a management plan in accordance with this part. In

cases in which SPR Therapeutics identifies a financial conflict of interest and eliminates it prior to the expenditure of PHS-awarded funds, SPR Therapeutics shall not submit an FCOI report to the PHS Awarding Component.

5.2.2. For any significant financial interest that SPR Therapeutics identifies as conflicting subsequent to SPR Therapeutics' initial FCOI report during an ongoing PHS-funded research project (e.g., upon the participation of an Investigator who is new to the research project), SPR Therapeutics shall provide to the PHS Awarding Component, within sixty days, a FCOI report regarding the financial conflict of interest and ensure that SPR Therapeutics has implemented a management plan in accordance with this work instruction. Where a FCOI report involves a significant financial interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed or managed by SPR Therapeutics (e.g., was not timely reviewed or reported by a subrecipient), SPR Therapeutics also is required to complete a retrospective review to determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research. Additionally, pursuant to paragraph 5.1.3.3 of this section, if bias is found, SPR Therapeutics is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

5.2.3. Any FCOI report required shall include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the financial conflict, and to assess the appropriateness of SPR Therapeutics' management plan. Elements of the FCOI report shall include, but are not necessarily limited to the following:

5.2.3.1. Project number;

5.2.3.2. PD/PI or Contact PD/PI if a multiple PD/PI model is used;

5.2.3.3. Name of the Investigator with the financial conflict of interest;

5.2.3.4. Name of the entity with which the Investigator has a financial conflict of interest;

5.2.3.5. Nature of the financial interest (e.g., equity, consulting fee, travel reimbursement, honorarium);

5.2.3.6. Value of the financial interest (dollar ranges are permissible: $0-$4,999; $5,000-$9,999; $10,000-$19,999; amounts between $20,000-$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value;

5.2.3.7. A description of how the financial interest relates to the PHS-funded research and the basis for SPR Therapeutics' determination that the financial interest conflicts with such research; and

5.2.3.8. A description of the key elements of SPR Therapeutics' management plan, including:

5.2.3.8.1. Role and principal duties of the conflicted Investigator in the research project;

5.2.3.8.2. Conditions of the management plan;

5.2.3.8.3. How the management plan is designed to safeguard objectivity in the research project;

5.2.3.8.4. Confirmation of the Investigator's agreement to the management plan;

5.2.3.8.5. How the management plan will be monitored to ensure Investigator compliance; and

5.2.3.8.6. Other information as needed.

5.2.4. For any financial conflict of interest previously reported by SPR Therapeutics with regard to an ongoing PHS-funded research project, SPR Therapeutics shall provide to the PHS Awarding Component an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan for the duration of the PHS-funded research project. The annual FCOI report shall specify whether the financial conflict is still being managed or

explain why the financial conflict of interest no longer exists. SPR Therapeutics shall provide annual FCOI reports to the PHS Awarding Component for the duration of the project period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component.

5.3. Remedies

5.3.1. If the failure of an Investigator to comply with SPR Therapeutics' financial conflicts of interest policy or a financial conflict of interest management plan appears to have biased the design, conduct, or reporting of the PHS-funded research, SPR Therapeutics shall promptly notify the PHS Awarding Component of the corrective action taken or to be taken. The PHS Awarding Component will consider the situation and, as necessary, take appropriate action, or refer the matter to SPR Therapeutics for further action, which may include directions to SPR Therapeutics on how to maintain appropriate objectivity in the PHS-funded research project. PHS may, for example, require SPR Therapeutics employing such an Investigator to enforce any applicable corrective actions prior to a PHS award or when the transfer of a PHS grant(s) involves such an Investigator.

5.3.2. The PHS Awarding Component and/or HHS may inquire at any time before, during, or after award into any Investigator disclosure of financial interests and SPR Therapeutics' review (including any retrospective review) of, and response to, such disclosure, regardless of whether the disclosure resulted in SPR Therapeutics' determination of a financial conflict of interest. SPR Therapeutics is required to submit, or permit on site review of, all records pertinent to compliance with this part. To the extent permitted by law, HHS will maintain the confidentiality of all records of financial interests. On the basis of its review of records or other information that may be available, the PHS Awarding Component may decide that a particular financial conflict of interest will bias the objectivity of the PHS-funded research to such an extent that further corrective action is needed or that SPR Therapeutics has not managed the financial conflict of interest in accordance with this part. The PHS Awarding Component may determine that imposition of special award conditions under 45 CFR 74.14 and 92.12, or suspension of funding or other enforcement action under 45 CFR 74.62 and 92.43, is necessary until the matter is resolved.

5.3.3. In any case in which the HHS determines that a PHS-funded project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not managed or reported by SPR Therapeutics as required by this part, SPR Therapeutics shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

6. Metrics

6.1. None

7. References

Document Number	Document Title
SPR-SOP-7.2.2	Initiation of a Clinical Investigation
SPR-SOP-7.2.4	Clinical Study Execution
SPR-FRM-7.2.2ac	PHS Funded Financial Conflict of Interest Disclosure Form

8. Revision History

Document Number	Author	Change Order	Description of Changes
SPR-WI-7.2.2f-1	Lechman	0012868	-Initial Document. Based upon NDI document WI-7.2.2f

SPR-WI-7.2.2f-2	Lechman	CHG-001753	Completed 3-year review. Added minor clarifications: • Removed reference to OLD policy that was a FRM document. Under previous NDI document management system "policy" was a form by the original author. Policy was then converted an NDI work instruction and NDI form. When converted to SPR document, reference to policy as form still existed. Removed now so that policy is this work instruction and form is specific PHS funded form. • added SFI acronym • clarified that department head, or designee, serves as Institutional Official since that is key term in regulation • clarified that individuals with FCOI will be made available following a written request (implied previously) and added 5 days following written request per regulation. • Replaced old references to NDI previously missed in conversion to SPR SOP. • Added reference to clinical execution SOP • Updated responsibilities to be specific with this procedure.
SPR-WI-7.2.2f-3	Haynes	CHG-003861	Completed 3-year review. Added minor clarifications: • Changed SRP Therapeutics in Section 3.7 to SPR Therapeutics • Updated the language in Section 5.1.3 to include required elements per the NIH checklist