ZALGEN LABS, LLC

RESEARCH INVESTIGATORS' FINANCIAL CONFLICT OF INTEREST POLICY FOR RESEARCH FUNDED BY THE UNITED STATES PUBLIC HEALTH SERVICE

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PURPOSE

It is critically important that research in the fields of science, engineering and medicine be conducted with complete objectivity. Responsible institutions engaged in research in these fields do their best to ensure that outside influences play no role in the outcome of their research studies. One way in which they do this is to attempt to ensure that no person in a position of trust in the institution has an unrecognized material outside financial incentive to intentionally introduce bias, error, fabrication or falsification into the work of the institution for which the person in a position of trust is responsible. If any such material outside financial interest is discovered, then the outside interest can be said to conflict with the institution's interest and the institution must manage the conflict of interest in such a way as not to allow the conflict to affect its research.

Regulations for researchers applying for and receiving Public Health Service ("PHS") funding have been promulgated. These regulations, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought" (42 CFR Part 50, Subpart F) and "Responsible Prospective Contractors" (45 CFR Part 94), are Research Investigators' Financial Conflict of Interest ("RIFCOI") regulations. As a recipient of PHS funds, it is the intent of ZALGEN LABS LLC to maintain and adhere to policies and procedures which comply fully with these regulations.

DEFINITIONS

RIFCOI Regulations are the Research Investigators' Financial Conflict of Interest regulations at 42 CFR Part 50, Subpart F, and 45 CFR. Part 94.

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

PHS means the Public Health Service of the HHS and any components thereof to which the authority involved may be delegated, including the National Institutes of Health ("NIH").

PHS Awarding Component means the organizational unit of the PHS that funds the research that is subject to the RIFCOI Regulations.

Institution means ZALGEN LABS, LLC ("ZALGEN" or "ZALGEN LABS")

Research means any research and development activity conducted by ZALGEN LABS that is funded by PHS grants, contracts or cooperative agreements.

Investigator means the project director ("PD") or principal investigator ("PI") and all other persons, if any, regardless of their title or position, responsible for the design, conduct or reporting of any Research.

Senior/Key Personnel means the PD/PI and any other persons identified as senior/key personnel by ZALGEN LABS in the grant application, progress report, or other report submitted to the PHS by ZALGEN LABS under the RIFCOI Regulations. Such individuals are Senior/Key Persons.

Institutional Responsibilities mean a person's responsibilities to ZALGEN LABS with respect to any Research.

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

Significant Financial Interest ("SFI") means any financial interest, other than a financial interest in ZALGEN LABS itself, of a person or the person's spouse or dependent children that reasonably appears to be related to the person's Institutional Responsibilities.

The RIFCOI Regulations stipulate certain thresholds of significance for financial interests in companies, trusts, and other entities. These thresholds, which do not apply to an interest in ZALGEN LABS itself, are as follows:

(a) If the entity is publicly traded, an SFI exists if a person receives more than $5,000 in remuneration from the entity in the twelve months preceding the disclosure, or if a person holds an equity interest in the entity which is valued at more than $5,000 as of the date of disclosure, or if such remuneration received plus such equity interest held total more than $5,000.

b) If the entity is not publicly traded, an SFI exists if a person receives more than $5,000 in remuneration from the entity in the twelve months preceding the disclosure or if a person holds any equity interest whatsoever in the entity, including any stock, stock options, LLC membership interest, or any other ownership right.

(c) If intellectual property rights and interests such as patent or copyright rights are involved, and if such rights and interests are in an entity other than ZALGEN LABS, then an SFI exists when a person receives any income related to such rights and interests.

(d) Paid Travel Expenses of any amount.

The term SFI is stipulated not to include the following types of financial interests:

(a) salary, royalties, or other remuneration paid by ZALGEN LABS to a person currently employed or otherwise appointed by ZALGEN LABS, including the value of intellectual property rights assigned to ZALGEN LABS and agreements to share in royalties related to such rights;

(b) any ownership interest in ZALGEN LABS;

(c) income from investment vehicles, such as mutual funds and retirement accounts, provided the person does not directly control the investment decisions made in these vehicles;

(d) 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 USC 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education; or

(e) income from services on advisory committees or review panels for a federal, state, or local government agency, an institution of higher education as defined at 20 USC 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.

Paid Travel Expenses are any travel expenses of an Investigator or Senior/Key Person which are reimbursed, sponsored, comped, waived, or otherwise paid for by any entity other than ZALGEN LABS for travel that is related to the Institutional Responsibilities of the traveler. Paid Travel Expenses are stipulated to be an SFI regardless of the dollar amount involved. An exception to this stipulation is travel expenses paid for by a federal, state, or local government agency, an institution of higher education as defined at 20 USC 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education. The details of any Paid Travel Expenses which must be reported to ZALGEN LABS include, at a minimum, the date, purpose, destination and duration of the travel and the identity of the entity which paid for it.

Research Investigators' Financial Conflict of Interest ("RIFCOI") means an SFI that could directly and significantly affect the design, conduct or reporting of Research. RIFCOIs occur in situations in which an SFI of Investigator or a Senior/Key Person compromise, could compromise, or could appear to compromise the professional judgment of that person regarding the design, conduct or reporting of Research. The bias an RIFCOI might conceivably introduce could affect choice of protocols, the collection, analysis and interpretation of data, the use of statistical methods, the hiring of staff, the procurement of materials, the disclosure of results, and other aspects of Research.

Institutional Official ("IO") is an official designated by ZALGEN LABS to solicit and review completed disclosure forms from each Investigator and Senior/Key Person who is planning to participate in or who is participating in Research. The IO(s) will consider the SFIs disclosed by the Investigators and Senior/Key Persons and determine whether any reported SFI is an RIFCOI.

RIFCOI Management Plan is a plan that specifies the actions that have been and will be taken to manage an RIFCOI.

ZALGEN LABS'S RESPONSIBILITIES REGARDING RIFCOIS

(a) ZALGEN LABS shall maintain an up-to-date, written, enforced RIFCOI policy that complies with the RIFCOI
Regulations and shall make such policy available via its Web site.

(b) ZALGEN LABS shall inform each Investigator and Senior/Key Person of its RIFCOI policy and of each such person's responsibilities regarding the RIFCOI Regulations and the disclosure of SFIs, and shall require each such person to complete adequate RIFCOI training

(i) prior to initially engaging in any Research,
(ii) at least every four years, and
(iii) immediately upon the occurrence of any of the following circumstances:

(1) ZALGEN LABS revises its RIFCOI policies or procedures in any manner that affects the requirements of Investigators or Senior/Key Personnel;

(2) An Investigator or Senior/Key Person is new to ZALGEN LABS; or

(3) ZALGEN LABS finds that an Investigator or Senior/Key Person is not in compliance with ZALGEN LABS's RIFCOI policy or management plan.

(c) If ZALGEN LABS carries out Research through a sub-recipient (e.g., subcontractors or consortium members), ZALGEN LABS shall take reasonable steps to ensure that any sub-recipient Investigator or Senior/Key Person complies with the RIFCOI Regulations by:

(1) Incorporating as part of a written agreement with the sub-recipient terms that establish whether the RIFCOI policy of ZALGEN LABS or that of the sub-recipient will apply to the sub-recipient's personnel.
(i) If the sub-recipient's personnel must comply with the sub-recipient's RIFCOI policy, the sub-recipient shall certify as part of the agreement referenced above that its policy complies with the RIFCOI Regulations. If the sub-recipient cannot provide such certification, the agreement shall state that sub-recipient Investigators are subject to ZALGEN LABS's RIFCOI policy for disclosing SFIs related to the sub-recipient's work for ZALGEN LABS;

(ii) Additionally, if the sub-recipient's personnel must comply with the sub-recipient's RIFCOI policy, the agreement referenced above shall specify time period(s) for the sub-recipient to report all RIFCOIs to ZALGEN LABS. Such time period(s) shall be sufficient to enable ZALGEN LABS to provide timely reports as required by the RIFCOI Regulations;

(iii) Alternatively, if the sub-recipient's personnel must comply with ZALGEN LABS's RIFCOI policy, the agreement referenced above shall specify time period(s) for the sub-recipient to submit all disclosures of SFIs to ZALGEN LABS. Such time period(s) shall be sufficient to enable ZALGEN LABS to comply timely with its review, management, and reporting obligations under the RIFCOI Regulations.

(2) Providing RIFCOI reports to the PHS Awarding Component regarding all SFIs of all sub-recipient personnel consistent with the RIFCOI Regulations, i.e., prior to the expenditure of funds and within 60 days of any subsequently identified RIFCOI.

(d) ZALGEN LABS shall designate one or more IOs to solicit and review disclosures of SFIs from each Investigator and Senior/Key Person who is planning to participate in or is participating in Research.

(e) ZALGEN LABS shall:

(1) Require that each Investigator and Senior/Key Person who is planning to participate in Research disclose to ZALGEN LABS's IO(s) their SFIs and those of their spouse and dependent children no later than the time of application for the Research.

(2) Require each Investigator and Senior/Key Person who is participating in Research to submit an updated disclosure of SFIs at least annually, in accordance with the specific time period prescribed by ZALGEN LABS, during the period of the award. Such disclosure shall include any information that was not disclosed initially to ZALGEN LABS pursuant to paragraph (e)(1) of this section, or in a subsequent disclosure of SFIs (e.g., any SFI identified on a PHS-funded project that was transferred from another Institution), and shall include updated information regarding any previously disclosed SFI (e.g., the updated value of a previously disclosed equity interest).

(3) Require each Investigator and Senior/Key Person who is participating in Research to submit an updated disclosure of SFIs within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new SFI.

(f) ZALGEN LABS shall provide guidelines consistent with the RIFCOI Regulations for the IO(s) to confirm that a disclosed SFI is related to Research, and if so related, whether the SFI an RIFCOI. An SFI is related to Research when ZALGEN LABS, through its IO(s), reasonably determines that the SFI (i) could be affected by the Research or (ii) is in an entity whose financial interest could be affected by the Research. The IO(s) may involve the Investigator or Senior/Key Person in the confirmation that an SFI is related to any Research. An RIFCOI exists when the IO(s) reasonably determine that the SFI could directly and significantly affect the design, conduct, or reporting of the Research.

(g) ZALGEN LABS shall take such actions as necessary to manage RIFCOIs, including any RIFCOIs of sub-recipient personnel pursuant to paragraph (c) of this section. Management of an RIFCOI requires development and implementation of a management plan and, if necessary, a retrospective review and a mitigation report pursuant to 42 CFR 50.605(a).

(h) ZALGEN LABS shall provide initial and ongoing RIFCOI reports to the PHS as required pursuant to 42 CFR 50.605(b).

(i) ZALGEN LABS shall maintain records relating to all Investigator and Senior/Key Personnel disclosures of FIs and SFIs and ZALGEN LABS's review of and response to such disclosures (whether or not a disclosure resulted in the determination of an RIFCOI) and all actions under ZALGEN LABS's policy or retrospective review, if applicable, for at least three years from the date the final expenditures report is submitted to the PHS or, where applicable, from other dates specified in 45 CFR 74.53(b) and 45 CFR 92.42 (b) for different situations.

(j) ZALGEN LABS shall establish adequate enforcement mechanisms and provide for employee sanctions or other administrative actions to ensure Investigator and Senior/Key Personnel compliance as appropriate.

(k) ZALGEN LABS shall certify, in each application for funding to which 42 CFR 50.604 applies, that ZALGEN LABS:

1) has in effect at ZALGEN LABS an up-to-date, written, and enforced administrative process to identify and manage RIFCOIs with respect to all projects for which Research funding is sought or received from the PHS;

2) will promote and enforce Investigator and Senior/Key Personnel compliance with this subpart's requirements including those pertaining to disclosure of SFIs;

3) will manage RIFCOIs and provide initial and ongoing RIFCOI reports to the PHS Awarding Component consistent with this subpart;

4) agrees to make information available, promptly upon request, to the HHS relating to any Investigator or Senior/Key Personnel disclosure of SFIs and ZALGEN LABS's review of and response to such disclosure, whether or not the disclosure resulted in ZALGEN LABS's determination of an RIFCOI; and

5) shall fully comply with the requirements of this subpart.

MANAGING RIFCOIS

(1) Prior to ZALGEN LABS's expenditure of any funds under a Research project, the IO(s) shall, consistent with 42 CFR 50.604(f), review all Investigator and Senior/Key Personnel disclosures of SFIs, confirm that such SFIs relate to Research and determine whether an RIFCOI exists. If an RIFCOI is determined to exist, ZALGEN LABS shall develop and maintain an RIFCOI Management Plan. Examples of conditions or restrictions that might be imposed to manage a financial conflict of interest include, but are not limited to:

- public disclosure of RIFCOIs (e.g., when presenting or publishing the research);
- for Research involving human subjects research, disclosure of RIFCOIs directly to participants;
- appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the Research against bias resulting from the RIFCOI;
- modification of the Research plan;
- change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the Research;
- reduction or elimination of the conflicting financial interest (e.g., sale of an equity interest); or
- severance of relationships that comprise financial conflicts.

(2) Whenever in the course of ongoing Research an Investigator or Senior/Key Person who is new to participating in the Research discloses an SFI or an existing Investigator or Senior/Key Person discloses a new SFI to ZALGEN LABS, the IO(s) shall within sixty days: review the disclosure of the SFI; confirm that it is related to Research; determine whether an RIFCOI exists; and if an RIFCOI is found to exist, implement, on at least an interim basis, an RIFCOI Management Plan. Depending on the nature of the SFI, ZALGEN LABS may determine that additional interim measures are necessary with regard to the Investigator or Senior/Key Person's participation in the Research between the date of disclosure and the completion of ZALGEN LABS's review.

(3) Whenever ZALGEN LABS identifies an SFI that was not disclosed in a timely manner by an Investigator or Senior/Key Person or, for whatever reason, was not previously reviewed during ongoing Research (e.g., was not reviewed or reported in a timely manner by a sub-recipient), the IO(s) shall, within sixty days: review the SFI; determine whether it is related to Research; determine whether an RIFCOI exists; and if so:

(i) Implement, on at least an interim basis, an RIFCOI Management Plan;

(ii) Whenever an RIFCOI is not identified or managed in a timely manner for reasons including failure by the Investigator or Senior/Key Person to disclose an SFI that is determined by ZALGEN LABS to RIFCOI, failure by ZALGEN LABS to review or manage such an RIFCOI, or failure by the Investigator or Senior/Key Person to comply with an RIFCOI Management Plan, ZALGEN LABS shall, within 120 days of ZALGEN LABS's determination of noncompliance, complete a retrospective review of the Investigator's or Senior/Key Person's activities and the Research to determine whether any Research or portion of Research conducted during the time period of the noncompliance was biased in its design, conduct, or reporting. ZALGEN LABS shall document such retrospective review and such documentation shall include, but not necessarily be limited to, all of the following key elements:

(1) Project number;
(2) Project title;
(3) PD/PI or contact PD/PI if a multiple PD/PI model is used;
(4) Name of the person with the RIFCOI;
(5) Name of the entity with which the person has the RIFCOI;
(6) Reason(s) for the retrospective review;
(7) Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed);
(8) Findings of the review; and
(9) Conclusions of the review.

(iii) Based on the results of the retrospective review, if appropriate, ZALGEN LABS shall update the previously submitted RIFCOI report, specifying the actions that will be taken to manage the RIFCOI going forward. If bias is found, ZALGEN LABS 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, a description of the suspected impact of the bias on the Research and ZALGEN LABS's plan of action or actions taken to eliminate or mitigate the effect of the bias (e.g., impact on the Research; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the Research is salvageable). Thereafter, ZALGEN LABS will submit RIFCOI reports annually, as specified elsewhere in the RIFCOI Regulations. ZALGEN LABS may design and implement such interim measures as are necessary to mitigate the effects of such an RIFCOI prior to the completion of ZALGEN LABS's retrospective review.

(4) Whenever ZALGEN LABS implements an RIFCOI Management Plan, ZALGEN LABS shall monitor Investigator or Senior/Key Person compliance with the management plan on an ongoing basis until the completion of the Research.

(5) (i) ZALGEN LABS shall ensure public accessibility via written response, to be mailed within five business days of a request, to any requestor of information concerning any SFI disclosed to ZALGEN LABS that meets the following three criteria:

(A) the SFI is still held by the Investigator or Senior/Key Person;
(B) ZALGEN LABS has confirmed that the SFI is related to the Research; and
(C) ZALGEN LABS has determined that the SFI is an RIFCOI.

(ii) The information that ZALGEN LABS makes available via such written response shall include, at a minimum, the following: the PHS project number; the Investigator's or Senior/Key Person's name, title and role with respect to the Research; the name of the entity in which the SFI is held; the nature of the SFI; and the approximate dollar value range of the SFI (dollar ranges are: $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 SFI is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value).

(iii) ZALGEN LABS will note in such 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 sixty days of ZALGEN LABS's identification of a new financial conflict of interest, which should be requested subsequently by the requestor.

(iv) ZALGEN LABS shall ensure that information concerning the SFIs of an individual subject to paragraph (a)(5) of this section shall remain available for responses to written requests for at least three years from the date that the information was most recently updated.

(6) In addition to the RIFCOIs that must be managed pursuant to the RIFCOI Regulations, ZALGEN LABS requires the management of other financial conflicts of interest in such manners as ZALGEN LABS deems appropriate.

REPORTING RIFCOIS TO PHS

(1) Prior to ZALGEN LABS's expenditure of any funds under a Research project, ZALGEN LABS shall provide to the PHS Awarding Component an RIFCOI report regarding any RIFCOI and shall ensure that ZALGEN LABS has implemented an RIFCOI Management Plan. In cases in which ZALGEN LABS identifies an RIFCOI and eliminates it prior to the expenditure of PHS-awarded funds, ZALGEN LABS shall not submit such an RIFCOI report.

(2) For any RIFCOI that ZALGEN LABS identifies subsequent to ZALGEN LABS's initial RIFCOI report during ongoing Research (e.g., upon the participation of an Investigator or Senior/Key Person who is new to the Research), ZALGEN LABS shall provide to the PHS Awarding Component within sixty days an RIFCOI report regarding the recently-identified RIFCOI and ensure that ZALGEN LABS has implemented an appropriate RIFCOI Management Plan. Pursuant to paragraph (a)(3)(ii) of this section, where such RIFCOI report involves an SFI was not disclosed in a timely manner or was not previously reviewed or managed by ZALGEN LABS (e.g., was not correctly reviewed or reported by a sub-recipient), ZALGEN LABS shall also complete a retrospective review to determine whether any Research conducted prior to the identification and management of the RIFCOI was biased in its design, conduct, or reporting. Additionally, pursuant to paragraph (a)(3)(iii) of this section, if bias is found, ZALGEN LABS shall notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

(3) Any RIFCOI report required under paragraphs (b)(1) or (b)(2) of this section shall include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the conflict and to assess the appropriateness of ZALGEN LABS's management plan. Elements of the RIFCOI report shall include, but are not necessarily limited to the following:

- Project number;
- PD/PI or Contact PD/PI if a multiple PD/PI model is used;
- Name of the person with the RIFCOI;
- Name of the entity with which the person has the RIFCOI;
- Nature of the financial interest (e.g., equity, consulting fee, travel reimbursement, honorarium);
- Value of the financial interest (dollar ranges are: $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);
- A description of how the financial interest relates to the Research and the basis for ZALGEN LABS's determination that the financial interest conflicts with such research; and
- A description of the key elements of ZALGEN LABS's RIFCOI Management Plan, including:
  (a) Role and principal duties of the conflicted person in the Research;
  (b) Conditions of the management plan;
  (c) How the management plan is designed to safeguard objectivity in the Research;
  (d) Confirmation of the Investigator's agreement to the management plan;
  (e) How the management plan will be monitored to ensure compliance; and

(f) Other information as needed.

(4) For any RIFCOI previously reported by ZALGEN LABS with regard to ongoing Research, ZALGEN LABS shall provide to the PHS Awarding Component an annual RIFCOI report that addresses the status of the RIFCOI and any changes to the RIFCOI Management Plan for the duration of the Research. The annual RIFCOI report shall specify whether the conflict is still being managed or explain why the conflict no longer exists. ZALGEN LABS shall provide annual RIFCOI reports to the PHS Awarding Component for the duration of the Research period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component.

(5) In addition to the RIFCOIs that must be reported pursuant to the RIFCOI Regulations, ZALGEN LABS requires the reporting of other financial conflicts of interest in such manners as ZALGEN LABS deems appropriate.

REMEDIES

(a) If the failure of an Investigator or a Senior/Key Person to comply with ZALGEN LABS's RIFCOI policy or an RIFCOI Management Plan appears to have biased the design, conduct, or reporting of any Research, ZALGEN LABS shall promptly notify the PHS Awarding Component of the corrective action taken or to be taken. ThePHS Awarding Component will consider the situation and, as necessary, take appropriate action, or referthe matter to the ZALGEN LABS for further action, which may include directions to ZALGEN LABS on how to maintain
appropriate objectivity in the Research. PHS may, for example, require institutions employing such aninvestigator or senior/key person to enforce any applicable corrective actions prior to a PHS award orwhen the transfer of a PHS grant(s) involves such individuals.

(b) The PHS Awarding Component and/or HHS may inquire at any time before, during, or after award
into any Investigator's or Senior/Key Person's disclosure of FIs and ZALGEN LABS's review (including any retrospective review) of and response to such disclosure, regardless of whether the disclosure resulted in ZALGEN LABS's determination of an RIFCOI. ZALGEN LABS is required to submit, or permit on site review of, all records pertinent to compliance with the RIFCOI Regulations. To the extent permitted by law, HHS will maintain the confidentiality of all records of FIs. On the basis of its review of records or other information that may be available, the PHS Awarding Component may decide that a particular RIFCOI will bias the objectivity of the Research to such an extent that further corrective action is needed or that has not managed the RIFCOI in accordance with the RIFCOI Regulations. 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 is resolved.

(c) 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 or Senior/Key Person with an RIFCOI that was not managed or reported by ZALGEN LABS as required by the RIFCOI Regulations, ZALGEN LABS shall require the Investigator or Senior/Key Person involved to disclose the RIFCOI in each public presentation of the results of the Research and to request an addendum to previously published presentations.