1. Overview

Clinical trials in biomedical research often requires complex interactions between industry, government, and others stakeholders. It is the role of Vivonics to ensure that these interactions do not result in the bias of research conducted at the institution. Additionally, it is a requirement of the United States Public Health Service (PHS) that any institution that receives or applies for PHS funding creates, maintains, an enforces a written conflict of interest policy that complies with the regulations of 42 C.F.R. Part 50, Subpart F. This regulation serves primarily to promote objectivity in research, as well as safeguard the public's trust in biomedical research funded and conducted by PHS and its affiliates.

2. Purpose

The purpose of this policy is to ensure that all research that is sponsored or conducted by Vivonics remains free of bias and is conducted in compliance with all relevant regulatory requirements. This document will outline the uniform set of standards by which Vivonics and its Investigators are required to disclose, manage, and report potential or real conflicts of interest.

3. Responsibilities

Role/Discipline	Responsibility
Clinical Manager	Executes and maintains policy
Investigator	Complies with policy

4. References:

Document #	**Title**
300-1-00002	Significant Financial Interest Disclosure Form

5. Glossary

The following terms, as they appear in this document, are defined below:

5.1. **Vivonics** refers to Vivonics, Inc., located at 175 Great Rd. Bedford, MA 01730.

5.2. **Conflict of Interest** refers to any situation in which an employee's personal interests may contradict that of Vivonics, or any scenario in which the objectivity of their research could be compromised or *appear to be compromised.*

5.3. **In-House Research** refers to any clinical trial or study conducted at any of Vivonics' facilities, or any research in which Vivonics qualifies as the Sponsor-Investigator, as defined by the International Organization for Standardization [ISO] 14155.

5.4. **Investigator** refers to the Principal Investigator and any other person, regardless of their job title, that is responsible for the design, conduct, or reporting of clinical research including subgrantees, contractors, consortium participants, collaborators, or consultants.

5.5. **Significant Financial Interest (SFI)** as it appears in this policy, is defined by the United States Public Health Services (PHS) as a financial interest held by the investigator and their spouse or dependent children, that meets the criteria below:

5.5.1. Remuneration received from a publicly traded entity in the 12 months preceding the disclosure and the value of any equity interest in the entity, which when aggregated, exceeds $5,000

5.5.2. Remuneration received from a non-publicly traded entity in the 12 months preceding the disclosure, which when aggregated, exceeds $5,000 or *any* equity interest in a non-publicly traded entity

5.5.3. Intellectual property rights and interests upon receipt of income related to such rights and interests (royalties that flow through the applicant organization are carved out and do not have to be disclosed)

5.5.4. Reimbursed or sponsored travel (travel reimbursed or sponsored by a federal, state, or local government is carved out and does not have to be disclosed)

5.5.5. Definition of SFI *excludes:*

5.5.5.1. Salary royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution;

5.5.5.2. Intellectual Property Rights assigned to the Institution and agreements to share in royalties related to such rights;

5.5.5.3. Any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization;

5.5.5.4. 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;

5.5.5.5. 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

5.5.5.6. Income from service on advisory committees or review panels for a federal, state or local government agency, Institution of higher education as defied 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.

5.6. **Financial Conflict of Interest (FCOI)** is any Significant Financial Interest (SFI) as defined above that could directly and significantly affect the design, conduct, or reporting of NIH/PHS-funded research.

6. Investigator Responsibilities

It is the responsibility of the Investigator to comply with their institution's policies and procedures. Investigators must disclose any Significant Financial Interests (as defined in the Glossary) held by themselves, their spouses, or their dependent children.

7. FCOI Training Requirements

Each PHS-supported Investigator is required to complete FCOI training. **(42 CFR 50.604(b))**
Vivonics Investigators must complete and obtain a certificate of completion from the Financial Conflict of Interest Tutorial put forth by the NIH Office of Extramural Research. https://grants.nih.gov/grants/policy/coi/tutorial2018/story_html5.html

This training must be completed:

- Prior to engaging in research related to any PHS-funded grant
- Every 4 years

- Immediately if:
    1. Vivonics revises its FCOI policy in such a way that affects the requirements or expectations of investigators
    2. An investigator is new to an institution
    3. The institution finds that an Investigator is not in compliance with the institutional FCOI policy or management plan

8. Disclosure

All Investigators are required to disclose any financial interest reasonably related to their institutional responsibilities held by themselves, their spouses, or their dependent children, that meets or exceeds the regulatory definition of a **Significant Financial Interest (SFI).** The calculation of these interests should be the aggregate amounts held by the Investigator, their spouse, and their dependent children.
This disclosure must occur: **(42 CFR 50.603, 42 CFR 50.604(e)(1)-(3))**

- No later than the time of application for PHS-funded research
- At least annually during period of reward
- Within 30 days of acquiring or discovering new SFI

Investigators are not required to submit a new disclosure before every application for PHS-funded research, *as long as there is an up-to-date disclosure on file at the institution.*

9. Review, Management, and Monitoring

An *individual/ committee designated by Vivonics* will solicit and review disclosures of SFIs and determine whether the disclosed interests could directly and significantly affect the design, conduct, or reporting or PHS-funded research, thus, whether the disclosed SFI is a Financial Conflict of Interest. **(42 CFR 50.604(d))**
This committee is responsible for:

- Developing and implementing a management plan within 60 days, as needed, to manage FCOIs **(42 CFR 50.605(a)(2)**
- Monitoring Investigator Compliance with the management plan until the completion of the project **(42 CFR 50.604(g), 42 CFR 50.605(a)(4)**

10. Non-Compliance

If an Investigator is found to be in non-compliance with the institution's policy or management plan, the institution will:

- Complete a retrospective review of investigator's activities and the PHS-funded research project to determine whether there was a bias in the design, conduct, or reporting of the research within 120 of determining non-compliance
- Document the retrospective review
- Submit a mitigation report to the NIH if bias is found

In any case in which the Department of Health and Human Services (HHS) determines that a PHS-funded clinical research project 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 an FCOI that was not managed or reported by the institution as required by the regulation, the Investigator involved is required to: **(42 CFR 50.606(c))**

- Disclose the FCOI in each public presentation of the results of the research and
- Request an addendum to previously published presentations

11. Reporting Requirements

Vivonics will submit initial and continuing FCOI reports to the NIH in accordance with the requirements of the regulation. **(42 CFR 50.604(h), 42 CFR 50.605(b))**
This must occur:

- Prior to expenditure of funds at start of project
- Within 60 days of new Investigator participating in project
- Within 60 days of newly identified FCOIs for all Investigators
- At least annually (at same time as when the institution is required to submit the annual progress report, multi-year progress report, if applicable, or at the time of a request for extension) to provide status of the FCOI and any changes to the management plan, if applicable, until the completion of the project
- Following a retrospective review to update a previously submitted report, if appropriate **(42 CFR 50.605 (a)(3)(iii)**

All FCOI reports are to be submitted to the NIH via the eRA commons FCOI module.

12. Maintenance of Records

(42 CFR 50.604 (i))
Vivonics will maintain all FCOI-related records, including but not limited to disclosure of SFIs or management plans for:

- At least 3 years from the date the final expenditures report is submitted to the PHS/NIH
- From other dates specified in **45 CFR 74.53 (b)** and **92.42 (b),** where applicable

13. Sub-recipients

Where applicable, Vivonics will:

- Establish via written agreement whether the subrecipient will follow their own institution's FCOI policy or the FCOI policy of Vivonics.
- Obtain certification from the subrecipient that the subrecipient institution's FCOI policy complies with the regulation
- Include in the written subrecipient agreement a requirement for the subrecipient to report identified FCOIs for its investigators in a time frame that allows the awardee institution (Vivonics) to report identified FCOIS to the NIH as required by the regulation

14. Conduct of In-House Clinical Trials

While FCOIs make up a large portion of the conflicts of interest that arise in biomedical research, not all conflicts are financial in nature. This section is included to specifically cover the responsibilities of Investigators during the recruitment and conduct of in-house research at Vivonics.

Investigators are expected to *avoid* the following conflicts of interest:

- Recruitment of immediate family members (including spouses, parents, children, siblings, grandparents, parents-in-law, or siblings-in-law) to participate in clinical studies or trials *unless it is specifically permitted by the IRB upon approval of the study*
- Recruitment of other Vivonics employees *unless it is specifically permitted by the IRB upon approval of the study*

  Note: In cases where the IRB has approved participation of Vivonics employees in Vivonics in-house clinical research, the consent process must include an explicit statement to informs the employee that their decision to participate or not participate in the study or trial is voluntary and will

in no way affect their continued employment at Vivonics or their relationship with individuals who may have an interest in the research.

15. References

United States, Department of Health and Human Services, Public Health Service. “Responsibility of Applicants for Promoting Objectivity in Research for Which PHS funding is Sought.” *Code of Federal Regulations*, Government Printing Office, 2011, pp. 180-183.

“Financial Conflict of Interest.” National Institutes of Health, U.S. Department of Health and Human Services, https://grants.nih.gov/grants/policy/coi/index.htm.

International Organization for Standardization. (2011). *Clinical investigation of medical devices for human subjects – Good clinical practice* (ISO/DIS Standard No. 14155). Retrieved from https://www.iso.org/standard/45557.html

Moore, Julie, and **Cristy McGoff**. 2019. "Conflicts of Interest in Human Subjects Research." *CITI Program* https://www.citiprogram.org.