

# A Prospective, Multi-Center, Non-Randomized Study to Evaluate the Quality of Life Impact After Treatment of Nasal Airway Obstruction Using the Aerin Medical Vivaer Stylus

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Study Sponsor:

**Aerin Medical Inc**  
 Primary Contact: Scott Wolf, MD, CMO  
 232 E. Caribbean Drive  
 Sunnyvale, CA 94089  
 Telephone: 650-605-3579

*A complete list of investigators will be maintained and will be available upon request.*

## SIGNATURES

### SPONSOR

Print Name: Scott Wolf, MD Title: CMO

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

### INVESTIGATOR

*I, the undersigned, certify that I have reviewed this Clinical Investigational Plan (CIP) and agree to abide by the terms of the study described herein and within the Investigator Agreement, Clinical Trial Agreement and according to the Declaration of Helsinki and The Belmont Report as well as any conditions imposed by the reviewing IRB, U.S. FDA or other regulatory agency.*

Print Name: \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

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## 1.0 PROTOCOL SYNOPSIS

<b>Study Title:</b>	A Prospective, Multi-Center, Non-Randomized Study to Evaluate the Quality of Life Impact After Treatment for Nasal Airway Obstruction Using the Aerin Vivaer™ Stylus
<b>Investigational Device:</b>	Aerin Medical Vivaer™ Stylus
<b>Subject Population:</b>	Male and female subjects who previously completed participation in the Aerin Medical Nasal Obstruction study
<b>Study Procedure:</b>	Subjects who have completed the Aerin Medical TP 258 study, "A Prospective, Multi-Center, Non-Randomized Study to Evaluate Treatment of Nasal Airway Obstruction Using the Aerin Medical Device." will complete the Nasal Obstruction Symptom Evaluation (NOSE) and a brief Aerin Medical Quality of Life Questionnaire
<b>Number of Sites:</b>	Up to 8 study sites
<b>Timepoints:</b>	From procedure: 12, 18 and 24 months

## 2.0 INTRODUCTION AND LITERATURE REVIEW

### 2.1 Introduction

The Aerin Medical Vivaer™ Stylus is a disposable handheld device capable of delivering bipolar radiofrequency energy to tissue and has been used to treat nasal airway obstruction.

Chronic nasal obstruction can elicit many symptoms, including congestion, stuffiness, headache, fatigue, sleep disturbance, daytime sleepiness, snoring and a decline in health-related quality of life (QOL) (Rhee, Book et al. 2003). In recent years, there has been growing awareness that nasal obstruction may impair various daily and social activities (Udaka, Suzuki et al. 2006) and result in a degradation of the patient's overall quality of life (Rhee, Weaver et al. 2010).

### 2.2 Subjective Assessment

Given the significant QOL impact of nasal obstruction, it is important to measure not only the physical symptoms (congestion, obstruction and ability to breathe) but also the impact of those symptoms on the patient's ability to sleep and the related consequences on rest, productivity, concentration and ability to participate in the normal daily activities of work and life.

In addition to the physical benefits of increased nasal patency, there are significant quality of life benefits that are associated with better breathing. After correcting nasal obstruction patients report significantly better sleep function (e.g. better night's sleep; lessened waking up during the night and difficulty falling asleep) as well as better psychological function (e.g. concentration, productivity and frustration). (Brown, Hopkins, et. al). We believe that these benefits may well be durable beyond the initial six months of the study in terms of sustained quality of life impact.

### 2.3 Study Design and Objectives

This is a prospective, non-randomized, multicenter follow-up study to collect long term data on a cohort of patients who participated in the Aerin Medical TP 258 study, “A Prospective, Multi-Center, Non-Randomized Study to Evaluate Treatment of Nasal Airway Obstruction Using the Aerin Medical Device.” The study will be conducted in a maximum of 8 centers. Follow-up data will be collected at the 12, 18 and 24-month post-procedure timepoints for all patients who have completed the above-mentioned study. The objective of the study is to evaluate the long-term durability of benefits associated with the Vivaer Stylus procedure.

### 2.4 Subject Population

The subjects in this study will all have completed participation in the TP 258 Nasal Obstruction study at each center. All subjects will be willing to and agree to participate. Of the original 50 patients in the pivotal trial, 49 would be eligible to participate.

### 2.5 Informed Consent Process

Patients who have gone through the Vivaer procedure and agree to participate in this follow-on study will be asked to sign an informed consent document.

#### Informed Consent

Informed consent will be obtained as outlined in 21 CFR Part 50 and the Good Clinical Practice: Consolidated Guidance (ICH, April 1996).

Prior to participation in the study, the patient or patient’s legal representative must sign an informed consent document.

### 2.6 Data Collection

Follow up data will be collected via telephone, by mail or during office visits. Data will be captured on a Follow-up Case Report Form (CRF).

### 2.7 Types of Assessments

After patients have had the opportunity to ask questions and receive answers, and the study informed consent form is signed, the following evaluations will be completed:

- The Study Staff will administer or ask that patients complete the Nasal Obstruction Symptom Evaluation (NOSE) scale and a brief Aerin Medical Quality of Life questionnaire. These tools can be administered either in the office, by mail or via a phone call.
- These tools will be administered at 12, 18 and 24 months ( $\pm$  6 weeks) after study treatment with the Vivaer Stylus

## 3.0 SUBJECT REIMBURSEMENT

Subjects may be reimbursed for their time spent completing the follow-up questionnaires and any expenses associated with each data collection time point, as allowed by study site policies. Subjects will not be reimbursed for incomplete questionnaires.

#### 4.0 STUDY WITHDRAWAL

Subjects may be terminated or withdrawn from the study for the following reasons:

- Voluntary withdrawal – meaning that the subject voluntarily chooses not to further participate in the study
- Lost to follow-up – meaning that the subject is more than one month late (beyond the late data collection window) and 3 documented attempts to contact the subject are unsuccessful. A subject who misses a follow-up time point but completes the questionnaires for a subsequent time point will no longer be considered lost to follow-up.
- In the physician's opinion, it is not in the best interest of the subject to continue study participation.
- Subject death.

Any study subject who does not complete the questionnaires for a specific data collection follow-up should be contacted by site personnel to determine the reason for the missed follow-up. The reason for the missed follow-up should be determined and documented in the subject's study records. All subjects enrolled (including those withdrawn or lost to follow-up) shall be accounted for with appropriate documentation.

#### 5.0 STUDY MANAGEMENT

This study will be conducted in accordance with elements of E6 Good Clinical Practice Consolidated Guidance, ICH, April 1996, Abbreviated Requirements of 21 CFR 812 for NSR device studies, the Declaration of Helsinki, the Belmont Report and any conditions imposed by the reviewing IRB or US FDA or other regulatory agency.

The study sponsor has the overall responsibility for the conduct of the study according to all applicable regulatory requirements. The study sponsor will have certain direct responsibilities and will delegate other responsibilities to the Principal Investigator. The study sponsor and Principal Investigator will ensure that the study is conducted according to all applicable regulations. All personnel to participate in the conduct of this clinical trial will be qualified by education and / or experience to perform their tasks.

The study sponsor, Investigator or any person acting for or on behalf of a sponsor or Investigator shall act in accordance the applicable standards, guidelines and regulations.

#### 6.0 REQUIRED DOCUMENTS FROM THE INVESTIGATOR (PRIOR TO STUDY START)

At a minimum, the following documents will be provided by the investigational site to the study sponsor:

- Signed Investigator Agreement
- Signed Clinical Investigational Plan (CIP) Signature Page
- IRB/EC approval
- IRB/EC approved Informed Consent Form (ICF)

- Investigator and Co-Investigator's current Curriculum Vitae
- Investigator and Co-Investigator's current Medical Licenses

A site may not begin study participation until all the above listed documents have been provided to the study sponsor.

Each study center will undergo protocol initiation including but not limited to a review of the following:

- Procedures for obtaining Informed Consent
- Procedures for completing Informed Consent Form
- Reporting requirements
- CRF completion and correction procedures
- Protection of patient confidentiality

## 7.0 ETHICAL CONSIDERATIONS

The rights, safety and wellbeing of clinical investigation subjects shall be protected consistent with the ethical principles outlined in the Declaration of Helsinki. This shall be understood, observed and applied at every step in this clinical investigation.

It is expected that all parties will share in the responsibility for ethical conduct in accordance with their respective roles in the investigation. The Sponsor and the Investigator shall avoid improper influence or inducement of the patient, study monitor, clinical investigator or other parties participating in or contributing to the clinical investigation.

## 8.0 PROTECTION OF PATIENT CONFIDENTIALITY

At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data shall be secured against unauthorized access. Privacy and confidentiality of information about each patient shall be preserved in the reports and in any publication. Each patient participating in this study will be assigned a unique identifier. All CRFs will be tracked, evaluated, and stored using only this unique identifier.

The investigational site will maintain a confidential study patient list (paper or electronic) identifying all enrolled patients. This list will contain the assigned study patient's unique identifier and name. The Site Principal Investigator (PI) bears responsibility for keeping this list confidential. This list will not be provided to the study sponsor and is only to be used at the study center.

Monitors and auditors will have access to the study patient list and other personally identifying information of study patients to ensure that data reported in the CRF corresponds to the person who signed the ICF and the information contained in the original source documents. Such personal identifying information may include, but is not limited to the patient's name, address, date of birth, gender, race and medical record number.

*NOTE: The patient's name, medical record number or address will NOT be recorded in the monitor's visit report or the database; demographic data that may be recorded includes age, race, and gender.*

Any source documents copied for monitoring purposes by the Sponsor will have patient identifiable information redacted and be identified by using the assigned patient's unique identifier in an effort to protect patient confidentiality.

## 9.0 DATA COLLECTION

Study data will be collected using standardized Case Report Forms (CRFs). The CRFs are designed to accommodate the specific features of the trial design. Modification of CRFs will only be made if deemed necessary by the study sponsor.

There is no source data for a questionnaire; the questionnaire itself is the source document.

## 10.0 STUDY SUSPENSION OR EARLY TERMINATION

The study can be discontinued at the discretion of the Site PI or Sponsor for reasons including, but not limited to, the following:

- Obtaining new scientific knowledge that shows that the study is no longer valid or necessary
- Insufficient recruitment of patients
- Persistent non-compliance with the protocol

If the study is discontinued or suspended prematurely, the Sponsor shall promptly inform all clinical investigator(s) / investigational center(s) of the termination or suspension and the reason(s) for this. The IRB/EC shall also be informed promptly and provided with the reason(s) for the termination or suspension by the Sponsor or by the Site PI / investigational center(s). Regulatory authorities and the personal physicians of the patients may also need to be informed if deemed necessary.

## 11.0 SITE CLOSE-OUT

At the time of the site close-out, the sponsor designee will collect all outstanding study documents, ensure that the Investigator's files are accurate and complete, review record retention requirements with the Investigator and ensure that all applicable requirements are met for the study. The observations and actions will be documented in a final closeout report.

## 12.0 RESPONSIBILITIES

Aerin Medical Inc. is the manufacturer of the Vivaer™ System and the Sponsor of this study. The study Sponsor has the overall responsibility of the study and will work to ensure compliance with

the Investigational Plan, elements of Good Clinical Practice: Consolidated Guidance (ICH, April 1996), signed study agreements and 21 CFR 812.2(b), *Abbreviated Requirements*.

The sponsor will be responsible for, but not limited to, conducting the following tasks:

- Select qualified Investigators
- Provide the Investigational Plan and any subsequent amendments
- Sign the protocol
- Provide appropriate information to Investigators and study site staff
- Promptly inform the Investigators and where applicable any regulatory authorities and Ethics Committees, if the study is prematurely terminated or suspended and the reason for the termination or suspension
- Provide protocol initiation training to include the Investigational Plan, CRF completion guidelines, and guidelines for obtaining informed consent
- Coordinate ongoing communication with consultants and study sites to resolve any problems concerning the protocol or data collection. Every effort will be made to ensure compliance with the protocol
- Retain ownership of all clinical data generated in this study, and control the use of the data for purposes of regulatory submissions to the US and other regulatory agencies
- Protect patient confidentiality
- Collect, store and keep secure, at a minimum, the following documents:
  - A current Curriculum Vitae and medical license of each Investigator
  - The name of the institutions where the study will be conducted
  - The IRB/EC opinion and / or approval, in writing, and relevant correspondence
  - Correspondence with authorities (as required)
  - Investigator Agreement
  - CIP Signature Page
  - Appropriate insurance certificates (as necessary)
  - IRB/EC Approved ICF
  - Names / contact information for study monitor(s)
  - Copies of signed and dated CRFs

### 13.0 SPONSOR MAINTENANCE OF STUDY RECORDS

The Sponsor will be responsible for **maintaining study records** per 21 CFR 812.140(b) and Good Clinical Practice: Consolidated Guidance (ICH, April 1996), Section 8.

The Sponsor will be responsible for **monitoring the investigation** per 21 CFR 812.46 and Good Clinical Practice: Consolidated Guidance (ICH, April 1996), Section 5.18.

The Sponsor will be responsible for **reporting** per 21 CFR 812.50(b).

#### 14.0 INVESTIGATOR MAINTENANCE OF STUDY RECORDS

The Site PI will be responsible for **maintaining study records** per 21 CFR 812.140(a) and Good Clinical Practice: Consolidated Guidance (ICH, April 1996), Section 4.9.

The Site PI will allow auditing of their clinical investigation procedure(s).

Each investigator will provide a completed Financial Disclosure prior to study initiation and upon request at later time points in the study.

The Investigator is responsible for maintaining medical and study records for every patient participating in the clinical study (including information maintained electronically such as digital imaging). The study center will also maintain **original** source documents from which study-related data are derived, which may include, but are not limited to:

- Clinic progress notes recording patient's medical history and medications
- Medical records regarding AEs, including treatment and clinical outcome
- Results of diagnostic examinations
- Notes of phone calls and/or correspondence indicating investigational site's attempts to contact and follow a study patient at the required follow-up time points until such time a subject is determined to be lost-to-follow-up.

The Investigator must ensure that all study patient records are stored for at least 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. To avoid error, the study site should contact the study sponsor prior to the destruction of study records to ensure that they no longer need to be retained. In addition, the study sponsor should be contacted if the Investigator plans to leave the investigational site so that arrangements can be made for the handling or transfer of study records.

#### 15.0 INVESTIGATOR REPORTS

The Site PI will be responsible for reporting per 21 CFR 812.150(a) and according to applicable IRB/EC requirements and Good Clinical Practice: Consolidated Guidance (ICH, April 1996), Section 4.11.

*NOTE: Reports must identify patients using the study's unique identifier to protect patient's confidentiality.*

The primary responsibility of the investigator is to protect the welfare of the study subjects. Other responsibilities, including adherence to the protocol, are defined in the Investigator Agreement.

#### 16.0 DATA MANAGEMENT

Data will be handled as applicable, per Good Clinical Practice: Consolidated Guidance (ICH, April 1996), Section 5.5. To ensure proper tracking of Case Report Forms, a tracking system will be utilized.

**16.1 Data Entry**

Qualified personnel assigned by the principal investigator and/or the sponsor will perform data entry.

**16.2 Data Back-up**

Incremental computer data backup will be performed on a regular basis. All hard copies of Case Report Forms and media will be stored in a secure location.

**16.3 Confidentiality and Security**

Passwords will be issued to appropriate personnel to insure confidentiality and protection of data.

**16.4 Final Report**

A final report will be completed, even if the study is prematurely terminated.

**16.5 Publication Policy**

After the conclusion of the trial, the results may be prepared and presented at a major meeting(s). The publication of results from any center experience within the trial is not allowed, unless there is written consent from the study sponsor.

**17.0 DEFINITIONS AND ACRONYMS****Case Report Form (CRF)**

Printed, optical or electronic document designed to record all the protocol required information to be reported to the sponsor on each trial subject

**Confidentiality**

Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or a subject's identity (GCP Consolidated Guidance).

**Ethics Committee (EC) / Institutional Review Board (IRB)**

Synonyms. An independent body constituted of medical, scientific and nonscientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects (GCP Consolidated Guidance).

**Good Clinical Practice (GCP)**

An international quality standard for conducting clinical trials that is provided by International Conference on Harmonisation (ICH) to protect trial subjects' rights, safety, and welfare, as well as provide integrity to the overall study data.

**Informed Consent**

The process by which a subject voluntarily confirms his or her willingness to participate in a trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to

participate. Informed consent is documented by means of a written, signed and dated consent form (GCP Consolidated Guidance).

**Informed Consent Form (ICF)**

A document disclosing the risks, benefits, and alternatives of a clinical trial and documents the subject's voluntary willingness to participate in a clinical trial.

**Source Data**

All information in original and identified records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. Source data are contained in source documents (ISO 14155 and GCP Consolidated Guidance).

**Source Documents**

Original documents, data and records (ISO 14155).

*NOTE: This may be, for example, hospital records, laboratory notes, pharmacy dispensing records, copies or transcriptions certified after verification as being accurate copies, photographic negatives, radiographs, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical investigation.*

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