Investigator Initiated Research (IIR) Proposal Submission Process

Introduction

Research is the lifeboat of medical innovation and Vapotherm is committed to collaborating with the medical community for the advancement of our technologies and related therapeutic application. While Vapotherm does periodically sponsor exploratory and definitive research through our Science & Innovation Department, we recognize that independent clinicians and researchers with a high academic understanding of Pulmonary Medicine and lung physiology will develop concepts for research independently from Vapotherm that align with our then-current needs.

The Investigator Initiated Research (IIR) program is not only designed to support independent research, but exemplifies the foundation for Vapotherm's Guiding Principles, maintaining a strong commitment to improving the lives of patients. Fully sponsored large-scale trials alone are often designed to demonstrate differentiation, validation or seek a particular outcome or collect information that will drive device labelling. Most companies do not have the human and or financial resources to conduct infinite large sponsored trials. Since sponsor-funded trials cannot be designed to evaluate all current and future uses of the device in patient care, the IIR program is designed to work and provide support for important research questions and hypotheses that Independent Investigators wish to explore. The IIR is a type of research where the investigator or the institution serves as the sponsor and Vapotherm provides support in the form of study device and/or disposables.

The IIR program begins with an idea, or a conversation among colleagues or with Vapotherm. It is designed to work and provide support for hypotheses generated by independent investigators that want to address a theory involving use of our technology that likely will not result in a sponsored trial. The value that these investigator-initiated trials bring to medicine is generally groundbreaking, practical and improve overall patient care.

This IIR pathway is made available to those working in healthcare as clinicians, clinician/researchers and bench researchers where our technology is utilized and studied IIR proposals are reviewed by Vapotherm's Clinical Research Committee and decisions are based upon scientific merit as well as alignment with Vapotherm's areas of research interest and the availability of resources.

Vapotherm encourages qualified clinicians and scientists to submit proposals to obtain needed support for Investigator-Initiated, site-sponsored research. The following important parameters apply to prospective applicants:

- Investigator-initiated research refers to projects that are conceived independently outside of Vapotherm. The application is for support in the form equipment loans and/or disposables.
- Vapotherm's research science committee will determine whether to award support based exclusively on (1) Vapotherm's then-current needs assessment in relation to the proposed research; and (2) Vapotherm's research resources availability in relation to the requested number of loan equipment and disposables. The decision of whether to award support will not be determined in a manner which takes into account the volume or value of referrals or business, if any, that may otherwise be generated between Vapotherm and the applicant.
- Any determination by Vapotherm to award support will be contingent upon the parties signing Vapotherm's research grant agreement in advance. The agreement will define the parties' rights and responsibilities with respect to the research grant, and provide in part that as the "sponsor" of the study, the investigator and/or the investigator's institution is solely responsible for obtaining IRB approval thereof.
- Vapotherm is a small, publicly held company. Not all applications for support can be granted, independent of interest and appropriateness of the study. It will be helpful to minimize the request for support to necessities as resources are limited.

Instructions for Submittal

Submit a complete research proposal based on the template described in the following section, which includes the detailed request for support (loaner equipment and/or disposable needs) and the proposed timeline for the research project. Only complete protocols can be evaluated for the necessary elements that govern our ability to provide support. Incomplete submissions will be returned.

Submit requests electronically via email at iir@vtherm.com.
Communications pertaining to your proposed investigation will be with the Science and Innovation and Legal teams at Vapotherm as opposed to your regional account managers and clinical managers.

You will receive a timely confirmation of your submittal and review of submission will take place at the subsequent regularly scheduled meeting of the committee.

Protocol Template (Only complete protocols will be subject to review)

- **Title page:** includes project title, anticipated study **timeline** (estimated start / completion dates), complete contact information for the Principle Investigator and a brief lay summary (abstract)
- **Background:** Provide a foundation for the project including description of foundational scientific and/or clinical information, as well as any preliminary work used to define the hypothesis
- **Specific Aims Page:** On no more than a single page, provide the precise, detailed descriptions for the **Objective** (pertaining to the overall research question), **Hypothesis** and **Specific Aims** for the project.
- **Study Design:** Description of the study model with mention of relevant elements such as design, target population, randomization scheme, etc.
- **Subjects:** Description of population to be studied and where/how they will be recruited, inclusion/exclusion criteria, and rational for statistical powering.
- **Procedures:** List detailed procedures for the study. Details should be adequate such that the data could be reproduced.
- **Data collection:** Describe each of the outcome parameters for each study endpoint and timeline for data collection
- **Plan for statistical Analysis:** Description of how the data will be analyzed to address the hypothesis and aims
- **References:** List any references cited in the background and protocol

Resource Request Form

Study Title: i.e. “High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial.”

Principal Investigator: i.e. John Smith, MD

Department Name and Location of Study Site:
i.e. Department of Pulmonary and Critical Care Medicine
Best Respiratory Care Ever Facility
100 Domain Drive
Exeter, NH 03833

Date Equipment Need by: 05/31/2020

Estimated Enrollment (N): 20

Equipment (Loan of Capital Units/Supply of Disposables)

Item Name	Description	Units Needed
Loaner Equipment	i.e. Vapotherm Precision Flow Plus Device	2
Disposable Supply	i.e. Adult Disposable Patient Circuit (DPC)	20
Disposable Supply	i.e. Adult Nasal Cannula—Large	20
Disposable Supply	i.e. Adult Nasal Cannula—Small Adult/Pediatric	10