



Vertex Investigator-Initiated Studies (IIS) Program Overview

Our Goal

To support independent, investigator-initiated research designed to advance scientific knowledge of disease states, patient populations, and medical treatment, in alignment with Vertex's clinical and nonclinical areas of interest

Types of Research Eligible for Support

Funding and/or drug support may be available for the following categories of research:

- Clinical studies involving INCIVEK™ (telaprevir) and ivacaftor*
- Observational studies that support research into hepatitis C and cystic fibrosis disease states, eg, epidemiological and outcomes studies
- Nonclinical studies using Vertex compounds for in vitro assays or in vivo models

* Ivacaftor clinical studies may not be initiated until after ivacaftor regulatory approval in the country where the study is to take place.

Research Programs of Interest

- Hepatitis C
- Cystic fibrosis
- Infectious disease*
- Oncology*
- Inflammation and immune-mediated disease*
- CNS disease, including pain*

*Nonclinical research only.

Review Criteria

Proposals will be evaluated in the following areas:

- Scientific rigor
- Innovation
- Feasibility
- Adherence to ethical principles
- Alignment with Vertex's overall research and development strategies
- Resource availability
- Reasonable cost

To be eligible for support, you must accept full responsibility for designing, conducting and monitoring your own studies.

Proposal Submission Process

You can apply to the IIS program using Vertex's online application system, located at:

www.vrtxiisgrants.com

For clinical research, the application is a 2-step process involving a preliminary concept proposal submission that, if accepted, is followed by a more detailed protocol submission. Nonclinical applications typically require a single submission.

Concept Proposal

A concept proposal is a brief, high-level outline of your study. It is not intended to be a complete abstract or protocol.

Nonclinical research applications require a single concept proposal submission. For clinical research, approved concept proposals require a subsequent detailed protocol submission, which then undergoes a second round of review.

Concept reviews are usually completed within 8 to 12 weeks. You will be notified of review decisions via e-mail. Following approval of a protocol, studies may not be initiated until a mutually acceptable grant or material transfer agreement has been executed.

Detailed Protocol

For clinical studies, if a concept proposal is approved, the next step is to submit a full protocol. A protocol is significantly more detailed and well developed, and is required only for clinical research applications.

Please be advised that submission of a protocol proposal does not guarantee eventual funding or materials.

Protocol reviews are usually completed within 60 days. You will be notified of review decisions via e-mail. Studies may not be initiated until a mutually acceptable grant agreement has been executed.

Study Budgets

Study budgets must be submitted at the time of concept submission and should be inclusive of all expected study costs. All budgets will be reviewed for accuracy and for alignment with fair market value.

Nonclinical study applicants must submit a comprehensive study budget at the time of concept submission. These budgets should include salary and benefits (as applicable), study supplies, statistical analysis, publication costs, animal costs and any other one time costs. Institutional overhead must be included.

Clinical study applicants must submit a detailed estimate of the study budget at the time of the concept submission. If your clinical concept proposal is approved, you will need to then submit a comprehensive line-item study budget. Please ensure that you include any start-up costs, salary support for all personnel, patient costs, laboratory fees, monies for publications, presentations, and associated travel and any other requirements. In an effort to ensure this can be done efficiently, we recommend that you start with the budget template provided at the top of the protocol submission Web page and amend it to reflect your protocol-related activities and institutional costs.

By submitting your budget, you are certifying that any overhead percentage indicated is consistent with your institutional guidelines. Please note that some costs, eg, publication costs, Institutional Review Board (IRB)/Ethics Committee (EC) fees, animal costs, etc are considered to be indirect study costs and are not subject to institutional overhead.

Review Process

If a nonclinical concept proposal is approved, Vertex will contact the Institutional Technology Transfer Office that you have listed in your application. A Material Transfer Agreement (MTA) will be drafted. Please note that studies may not be initiated until a mutually acceptable MTA has been executed.

If a clinical concept proposal is approved, you will be instructed via e-mail to log in to the Vertex IIS Web site and submit a full protocol. The protocol then undergoes a second review cycle. If the protocol receives final approval from the Investigator Initiated Studies (IIS) Review Committee, Vertex will contact the legal department or contracts office that you have listed in your application to begin negotiating a grant agreement. Please note that studies may not be initiated until a mutually acceptable grant agreement has been executed.

Initiation Requirements

If your nonclinical concept is approved, Vertex will require a fully executed MTA and documentation of Institutional Animal Care and Use (IUCAC) approval, if appropriate, prior to study initiation.

If your clinical protocol is approved, Vertex will require documentation of IRB/EC approval, a copy of the IRB/EC approved final protocol, confirmation of regulatory authority approval (if applicable), and a fully executed grant agreement prior to study initiation.

Regulatory Responsibilities (Clinical Research)

As the study sponsor, you must ensure that the study is conducted in accordance with all applicable regulatory requirements, including adherence to International Conference on Harmonisation (ICH) and Good Clinical Practice (GCP) guidelines. You must assume all regulatory responsibilities including but not limited to IRB/EC approvals, regulatory authority approvals, and any associated reporting obligations to regulatory authorities.

If a study utilizes a product in a way that is not consistent with the approved product label, you, as the study sponsor, must file an application with the relevant regulatory authority, eg, an Investigational New Drug (IND) application to the FDA or a Clinical Trial Application (CTA) to Health Canada. Vertex will provide necessary supporting documentation for IND/CTA filings in the form of a cross-reference letter. For further guidance relating to these applications, please refer to the document, "Regulatory Authority Submission Information," on the protocol submission Web page for links to the relevant regulatory authority Web sites.

Study Maintenance

If your clinical protocol is approved and a contract is fully executed, you will need to submit quarterly study progress updates. This will require that you describe, in specific and quantifiable ways, the current status of your protocol (eg, 40 subjects enrolled, 12 focus groups held, 200 charts reviewed). Updates must be entered whether or not there has been a change in status. At this time, you should also report any publications, continuing approvals, and study amendments since your last report.

Protocol Amendments

All amendments to study protocols must be submitted to and approved by Vertex prior to submission to the IRB/EC or governing regulatory authority. Documentation of subsequent IRB/EC and regulatory approvals must be submitted to Vertex.

Safety Reporting Requirements (Clinical Research)

If your study involves the use of a Vertex drug, you will be required to follow Vertex's safety reporting requirements.

You must report any serious adverse event (SAE) to Vertex within 24 hours of first knowledge. In accordance with 21 CFR 312.32, a SAE is an adverse event 1) Associated with the subject's death; 2) Associated with inpatient hospitalization or prolonged hospitalization of the subject; 3) Life-threatening to the subject; 4) Associated with severe or permanent disability; 5) Associated with a congenital anomaly or birth defect; or 6) Associated with an event which appropriate medical judgment determines may require medical or surgical intervention to prevent one of the outcomes listed above.

SAEs can be reported using the SAE Reporting Form provided by Vertex, Medwatch Form 3500A or another appropriate regulatory form.

Reports should be submitted to Vertex Global Patient Safety at:

globalpatientsafety@vrtx.com

All adverse events (AEs) occurring during the study and possibly related to the study drug must be reported to Vertex in aggregate on an annual basis, ie, provide a copy of the Annual Report submitted to the FDA.

These requirements will also be set forth in the contract between Vertex and your institution. Reporting to Vertex does not relieve you of your reporting obligations to your IRB/EC or Regulatory Authority. **Vertex will not report AE/SAEs to your Regulatory Authority on your behalf.**

Payment Information

Payments are linked to the achievement of study milestones laid out in the MTA or grant agreement. In order to receive a payment associated with a particular milestone, you must submit an invoice to our Accounts Payable department. Invoices can be submitted via e-mail to:

Accounts_Payable@vrtx.com
and cc: vrtx_iisgrants@vrtx.com

or mailed to:

Vertex Pharmaceuticals
P.O. Box #390569
Cambridge, MA 02139
United States

Drug Supply

Vertex will supply study drug in accordance with the terms of the MTA or grant agreement. Study drug must be used solely in the study and may not be made available to any other party. Drug remaining at the completion of the study must be destroyed according to institutional policy and documentation of its destruction must be provided to Vertex.

Nonclinical material shipments will be made upon the receipt of a fully executed MTA and according to the agreed upon schedule.

For clinical studies, unless otherwise specified, study drug will be supplied in the approved commercial packaging. Any study-specific labeling is the responsibility of you, as the study sponsor. Secured storage, drug accountability, etc, are also your responsibility as study sponsor.

The initial clinical drug shipment will be made upon receipt of a fully executed grant agreement, IRB/EC approval, a copy of the IRB/EC approved protocol, documentation of IND/CTA receipt (as applicable), and verification of pharmacy licensure.

Additional clinical drug shipments will be made depending on subject enrollment. You can request additional shipments through the online application and study management Web site.

Closeout Requirements

Vertex requires a final written report documenting study results at the conclusion of each investigator-initiated study. Details regarding this requirement will be described in the grant agreement. At the conclusion of the study, it will also be necessary to provide Vertex with a financial reconciliation of funds provided and documentation of the destruction of any remaining study drug.

Publications

Vertex encourages the publication of study results. As noted above, we require in our contracts that manuscripts, abstracts and presentations first be submitted to Vertex, in advance of their submission, for courtesy review and to allow for protection of intellectual property rights.

Financial Disclosure

Vertex may publicly disclose funding associated with IIS support.

Application Assistance

For questions regarding the Vertex IIS Program, please contact:
vrtx_iisgrants@vrtx.com.