

Investigator Sponsored Trial (IST) Guidelines for Investigators

IST Approval Process

The IST Review Committee (IRC) is the Agios committee responsible for reviewing all IST concepts and protocols that are submitted by the Investigator for support. Below are the detailed steps taken as new IST concepts are reviewed, approved and activated. It is our hope that these guidelines will assist you as you develop and implement your new study ideas.

Concept

- **Discuss** your new concept with your Agios Medical Science Liaison (MSL).
- Your MSL will inform you if this concept is of scientific interest to Agios.

Concept Submission

- **Submit formal Concept**, proposed itemized budget (if applicable), and Investigator Curriculum Vitae to Agios via VisionTracker: https://agios.envisionpharma.com/vt_agios/
- A worksheet to assist with your concept entry into the system can be found under **IST Information**.
- Your proposal will be **reviewed by the IST Review Committee (IRC)**. The committee will decide if your concept is approved, determines support, and assembles feedback for the Investigator.
- **If your concept is approved**, you will receive written notification of the approval. This will include details on the type of support Agios has approved and feedback on your concept.
- You will be **required to sign** an Agios specific Confidentiality Agreement (**CDA**) at this time.
- Once the CDA is executed, the Investigator's Brochure will be sent to you.

Draft Protocol

- **Submit your Draft Protocol in Visiontracker (VT)**, detailed budget (if applicable) and supporting documents to Agios within **60 days** of receiving the notification of Concept Approval.
- The protocol will be reviewed at the next IRC meeting. Feedback will be provided as follows:
 - **Protocol Not Approved**
 - **Protocol Approved**
 - **Protocol Approved with Modifications:** Communication is sent detailing Agios' suggestions and recommendations for your final protocol

Final Protocol

- **Submit your Final Protocol and Final Budget** (if applicable) to Agios through VT within **30 days** of receiving Agios feedback on your protocol.
- **If the protocol is approved as final**, you will be notified of final protocol approval. Agios will confirm the support, will provide a **contract**, and will ask the **Investigator to submit** an Investigational New Drug (IND) Application to the FDA or Clinical Trial Application (CTA) or equivalent as applicable to your Country's Health Authority as applicable.
- **Submit** the final Agios approved protocol, informed consent form and supporting documents **to your IRB/Ethics Committee for approval**.

Regulatory Documents

- **Submit the following regulatory documents** to Agios through Visiontracker within **60 days** of being notified that your protocol has been approved:
 - Final IRB/EC Approval of the final protocol and informed consent
 - FDA or Country's Health Authority submission and approval if applicable indicating your study can proceed
 - FDA 1571 / 1572 forms or Country equivalent and other documents as required
 - Signed Investigator's Brochure Acceptance Form

Contract

- **Final Investigator Sponsored Trial Contract execution** should take place within **60 days** of receiving a draft contract at your institution. Contact Agios immediately if there are delays.

Trial Activation

- The trial **cannot begin until** Agios has confirmed receipt of **all** required regulatory documents, the final IST contract is signed by all parties and you have received notification from Agios that the trial is activated.
- Agios provides supply request forms for drug shipment & requests invoices for payments (if applicable).
- All documents should be uploaded directly in the VT system.

Trial Execution

- The study should enroll at least one subject/month, depending on the indication and study design. **If there is an issue or delays with enrollment**, please contact Agios.
- **Enrollment updates and study status** should be submitted to Agios on a **monthly** basis through Visiontracker.
- **Annual IRB/EC Approval letters, all FDA or Country specific Health Authority correspondence and Annual IND Reports or equivalent** (if applicable) must be shared with Agios through Visiontracker.
- **Protocol amendments MUST** be submitted to Agios and proceed through Agios IRC review for approval **before** submission to your IRB/EC for review and changes are implemented.

Trial Close Out

- Please discuss your expected completion, publication and final report timelines with Agios.
- **Submit** copies of **notification of study closure** with FDA/Health Authority and IRB/IEC.
- Submit **final invoice** and drug accountability (if applicable)