Instructions for Submission of Investigator-Initiated Trials and General Guidance

The following are instructions for Investigators wishing to submit a proposal for an Investigator-initiated Trial (IIT) and general Halozyme guidelines for conduct of IITs.

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1. PURPOSE
The mission of the Halozyme Investigator-Initiated Trial (IIT) Program is to provide support for Investigators-initiated research that advances medical and scientific knowledge about Halozyme products and generate promising medical therapeutics. The program is open to all researchers who are interested in receiving partial support for conducting their own research.

Types of Research Eligible for Support include clinical studies of approved and potential new uses, involving approved or investigational Halozyme drugs

Support is typically provided in the manner of funding, and/or drug depending upon the type of research.

2. SUBMITTING AN IIT PROPOSAL
Halozyme accepts Concept Proposal submissions from Investigators-initiated trial grant requests. If a Concept Proposal is of interest, a follow-up request for a Full submission will be made by Halozyme. A Full Submission must be received in order for a request to be considered for approval.

Please submit requests and any questions regarding the submission process to Requests@halozyme.com

Halozyme will acknowledge receipt of all grant submissions. The review process is conducted by a Concept Review Committee and decisions are based upon medical and scientific merit as well as the available resources and research priorities. Halozyme will make every attempt for a speedy review process and communicate the process timelines along the way with the Investigator and/or representative. A formal notification on the status of your application will be sent once a decision is reached. While all requests will be reviewed, Halozyme makes no promises that it will approve a request.

3. CONCEPT PROPOSAL
A Concept Proposal Form and instructions will be provided at your request.

A Concept Proposal should contain an adequate amount of information in order for Halozyme to determine interest in receiving a Full Proposal. When submitting a Concept Proposal, the following information is requested:

- Clinical site information including Principal Investigator (please include medical license number) and information for the contact person
- Project description including hypothesis and objectives, study title, phase of research, population, treatment regimen, enrollment and approximate study dates
- Draft itemized budget including other support not requested in the proposal to support the study
- Amount of product required
- Curriculum Vitae of the Investigator
4. **FULL SUBMISSION**
A Full Proposal submission must contain enough detail about the research study and the grant request to enable Halozyme to make a final evaluation regarding support. When submitting a Full Proposal, the following information will be requested:

- Full Protocol
- Draft Informed Consent Form
- Total funding requested (itemized and detailed)
- Curriculum Vitae of any sub-investigators and other clinical staff expected to participate in the study
- Certification that no one to be involved in the investigation had been disqualified, debarred or otherwise under investigation by a Regulatory or Institutional body.

5. **BUDGET**
Before submitting your budget, please ensure that all study-related expenses have been itemized and are appropriate with fair market value.

Halozyme will consider funding activities related to both direct (subject-related costs, study-related personnel costs, diagnostic fees/services and external data management expenses, etc.) and indirect study costs (e.g., IRB review fees, equipment and supply expenses).

Halozyme will not compensate for the following: general education or training activities, support for ongoing clinical programs that are part of an organization’s routine operations, start-up funds to establish new clinical or research programs or to expand existing programs, purchase of capital equipment unrelated to the study or that would generate revenue, construction funds or hiring of staff that are not dedicated to the study.

6. **HALOZYME REQUIREMENTS FOR IIT COLLABORATION**
Upon approval of the Full Proposal, there are several documents that are required prior to initiating support (drug and/or funding). These include:

- Final Study Protocol and Informed Consent Form
- IRB/ethics committee approval letter of final Study Protocol and Informed Consent
- Submission/approval of regulatory documents (IND, CTA, or other applicable regulatory approvals) and with commitment to comply with regulatory requirements
- Fully executed Grant Agreement

Halozyme requires at least one study status update per quarter unless otherwise specified to comply with Halozyme-required regulatory requirements. Updates should include information on enrollment, adverse events (AEs), projected publications and study completion dates. Additional requirements for the provision of safety information to Halozyme is included in Section 7. Halozyme also requires notification of any amendments to the original protocol after the study has been initiated.

An Investigator conducting an IIT is required to provide Halozyme with a written report of the final study results. Any planned publications or presentation must be sent to Halozyme in
advanced of submission according to the Grant Agreement. Upon study closure, the Investigator will be required to certify that the study was conducted and the Halozyme funds and/or drug were used solely to conduct or report the study and that all safety and regulatory reporting obligations were met. Any unused funding and drug must be returned to Halozyme within 90 days of study completion.

7. SAFETY REPORTING
Halozyme has the ethical and legal responsibilities to collect and analyze safety information on its investigational and marketed products so that the company can fully understand their risk-benefit profile and provide accurate safety information to regulatory authorities, physicians and patients. As an independent Investigator-sponsor conducting research involving Halozyme products, you play an important role in monitoring the study and reporting all safety events to Halozyme.

A cumulative listing of adverse events must be provided to Halozyme on a quarterly basis or sooner to comply with Halozyme-required regulatory submissions. This listing should include all adverse events that have occurred from the start of the study.

For serious AEs (SAEs), initial notification of the event must be provided to Halozyme within 24 hours of the Investigator’s initial awareness. The initial notification should include a description of the event, subject number/initials, criteria for seriousness, severity, assessment of relationship to study drug(s), whether the event was expected or unexpected per the Investigator’s Brochure or Package Insert, and other available information relevant to the event. If the SAE meets regulatory reporting criteria for a 7-day or 15-day report, the final MedWatch/CIOMS report, including follow-up reports, must be provided within 15 calendar days from initial awareness of the event or receipt of new information about a previously reported event. For periodic reports (i.e., reports for SAEs that don’t meet 7-day or 15-day reporting criteria), the draft or final narrative or MedWatch/CIOMS report must be provided within 30 calendar days of initial awareness or receipt of new information. Final versions of SAE reports/narratives for periodic reports must be provided to Halozyme within 30 calendar days after closure of the study database.

Reporting an AE or SAE to Halozyme does not relieve the institution and/or Investigator of the responsibility for reporting the events to the FDA, other regulatory authorities, or IRB/EC, as required per relevant local and federal regulations.

For definitions, references, and additional information, please refer to the Instructions for Safety and Regulatory Reporting for Halozyme’s guidelines for conducting an IIT.

8. INVESTIGATOR RESPONSIBILITIES
As the sponsor of a study, the Investigator and/or Institution must ensure that the study is conducted in accordance with the provision of the ICH GCP Guidelines and all applicable local and regulatory requirements. The Investigator must assume all regulatory responsibilities including, but not limited to, IRB/EC approvals, informed consent, regulatory approvals, and any and all reporting obligations to local regulatory authorities.
9. PUBLICATIONS
Halozyne encourages Investigators to publish the results of the study, whether or not the results are favorable to the Halozyne product. The Investigator will comply with recognized ethical standards concerning publications and authorship such as those established by the International Committee of Medical Journal Editors. Halozyne reserves the right to first review of any draft publications.

10. REGISTERING YOUR RESEARCH WITH PUBLIC WEBSITES
The Investigator and/or Institution must add the study to the FDA’s ClinicalTirals.gov database or a trial registry website in the country of study.

11. INDEMNIFICATION
Halozyne requires that the Institution indemnify Halozyne. Details will be outlined in the Clinical Trial Agreement.

12. FINANCIAL DISCLOSURE BY HALOZYME
If applicable, as a publically traded company, Halozyne is dedicated to transparency relating to its financial relationships with Investigators and study sites; therefore Halozyne may publically disclose funding associated with an IIT.