

Shire's Investigator Initiated Research (IIR) System and Process FAQs

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General Information:

IIR Mission and Purpose

Shire is committed to broadening medical and scientific knowledge pertaining to its products, disease states of interest and medical practice (e.g., advancement of basic research, and enhancement of disease understanding and/or clinical outcomes) through the provision of material and/or financial support in the form of IIR grants.

Eligibility

IIR grants are not provided to individuals. Only institutions/organizations are eligible to receive IIR grant support from Shire. Potential IIR grant recipients include universities, medical schools, hospitals, academic medical centers, physician groups organized as a legal entity, hospice centers, research foundations, government departments and agencies that are authorized to receive funds for research.

Shire will review requests from independent researchers who have the necessary scientific background and experience to conduct an independent scientific investigation for a specific research project.

General Principles

In an effort to advance research and enhance understanding of disease, Shire supports **independent** research relating to disease areas of interest (AOIs) to Shire or relating to Shire's products.

Shire responds to **unsolicited** requests for support of IIR studies through its IIR program. IIR investigators and/or their affiliated institutions assume responsibility for all aspects of the study, including design, regulatory approval, initiation, conduct, monitoring, analysis and publication of study results.

Areas of Interest (AOI)

Shire's current AOIs can be found at <https://www.shire.com/research-and-development/investigator-initiated-research/areas-of-interest>.

Will Shire provide operational support for my IIR?

Shire does not provide operational support (e.g., authorship of a protocol, statistical analysis, study report, publication, site monitoring) for an IIR. Operational support of an IIR is the responsibility of the Investigator.

System Access

How do I register?

Click on the "Register" button on the login page of Shire's Investigator Initiated Research (IIR) grant management system at <https://ist.shiresupport.com/Shire-IIS-PROD/>. Complete and submit the required information. You will receive an e-mail acknowledgement from Shire within 24 hours confirming the new account.

Note: if you do not receive a confirmation email please contact IIRSupport@shire.com. In some cases, the emails may be rejected by your institution as spam.

Why was I prevented from registering?

Common reasons include:

- Some of the information entered as part of your registration was not valid. Please look for any error messages and re-enter corrected information in the requested format.
- You entered an e-mail address during your registration that has already been registered in the system.

If you experience continued problems please contact Shire at IIRSupport@shire.com.

Why doesn't my login and password work?

If you have forgotten your password, you may reset your password by clicking the "Forgot Password" link. If you are still unable to access the system, please contact IIRSupport@shire.com.

If you are not able to login due to account inactivity please contact IIRSupport@shire.com.

Can multiple investigators use the same account to submit IIR requests to Shire?

No, each individual investigator who would like to submit a research request to Shire must have his or her own account within the system.

What if I enter false information?

Providing false information or failing to answer all questions truthfully and completely may be grounds for not accepting the request, halting existing requests, or excluding organizations from participating in Shire's IIR program. Falsifying an application, attempting to violate the privacy of others, or attempting to compromise the operation of the system may also be punishable by law.

IIR Submission

What types of research proposals are eligible for support by the Shire IIR program?

Both clinical (interventional and observational) and preclinical studies (in vitro and animal) are eligible to be considered for IIR support.

IIR support can be provided in the form of financial support, product supply or both.

Does the IIR program support product requests not directly related to a protocol-based research proposal?

No.

How do I submit a proposal?

IIR grant requests must be submitted through the Shire IIR Management System at <https://ist.shiresupport.com/Shire-IIS-PROD/> to be eligible for consideration. Requests received via email or traditional mail will not be considered.

What is the difference between a “brief” and “full” proposal?

You may choose to submit either a brief (concept) or full proposal. A brief proposal requires limited information which can be used to gauge Shire’s interest in the research study. If a brief proposal is approved, the investigator is invited to submit a “full” study proposal for further review and consideration. Approval of a brief does not guarantee approval of the subsequent full proposal. Brief proposals are reviewed on ongoing basis (standard review timeline 45 days) and Full proposals quarterly.

A full proposal requires detailed study information and detailed budget.

Funding/product support decisions can only be made upon Shire`s review of a full proposal

Please refer to <https://www.shire.com/research-and-development/investigator-initiated-research/review-cycle> for details regarding Shire’s IIR Review Cycle.

What information is required for submitting a “brief” proposal and a “full” proposal?

	Brief Proposal	Full Proposal
Basic Study Information	<ul style="list-style-type: none"> • Study title • Hypothesis • Overall Project Cost • Primary Investigator CV 	<ul style="list-style-type: none"> • Study title • Background/Rationale • Hypothesis • Medical License Number for Physicians and Primary Investigator CV •
Study Details and Design	<ul style="list-style-type: none"> • Primary Objective • Brief Inclusion and Exclusion Criteria Sample size if applicable • Estimate of the total budget <p>Note: Additional documents can be uploaded as needed</p>	<ul style="list-style-type: none"> • Brief Inclusion and Exclusion Criteria • Primary Objective • Study Design: • Number of Sites • Experimental Design • Additional Study details, including estimated recruitment period and study timelines • Study Event Information: Treatment information, drug supply requirements (if applicable), statistical analysis plan, etc. • Itemized, Detailed Budget that are commensurate with Fair Market Value (FMV) and includes all study-related expenses: • Direct Study Costs • Indirect Study Costs (e.g. overhead costs.) <p>Note: Additional documents can be uploaded as needed</p>

Notes related to IIR Budget:

1. Shire's standard rate for overhead is 25% of the total direct study costs. Overhead will not be paid on indirect study costs (publications and research/ethics related fees or travel related costs).
2. Shire may support reasonable publication submission and/or review fees, and modest and reasonable travel expenses related to study updates and poster presentations up to 2,500 USD, as long as they are budgeted and noted in the agreement;
3. Shire does not support cost to purchase durable equipment, but may support reasonable leasing costs for such equipment to be used for the sole purpose of the requested IIR;
4. Shire will not compensate for the following costs:
 - Costs for research performed in the past
 - General educational and training activities costs
 - Costs for activities that are part of an organization's routine operations and are not specific to the particular IIR
 - Purchases of capital or durable equipment unrelated to the IIR
 - Hiring of staff that are not dedicated to the IIR

What if my descriptions, study objectives, etc. do not fit into the allotted space?

A high-level summary is required within the allotted space. If the provided space is not enough for you to enter complete/detailed description, it is recommended that you upload detailed supporting documentation at the end of the Request Form..

What does a Request for Additional Information (RAI) mean and how much time do I have to respond?

A "Request for Additional Information" (RAI) is made when supplementary information or clarifications are needed to assist in considering the request. The RAI will be sent via e-mail to the registered e-mail address provided by the requestor. Please review the e-mail carefully and submit the additional information through the system by logging in and clicking on the "Please submit additional information" link next to the applicable IIR request. If Shire has not received the necessary information within 90 calendar days of the request for additional information, the original request may be closed.

May I complete a portion of the online application and come back to it later?

Yes. If you are unable to complete your online application in one session, you may save it and come back to it later by clicking "Save & Continue Later" at the bottom of the page. At any time prior to submitting, you will have the opportunity to come back and make changes to the application. As you enter the information, please click "Save" on the page often to preserve the information you have entered, as the system does time out due to inactivity and you may lose information entered if you did not save it timely.

May I submit an IIR proposal if I already have one approved by Shire?

Yes. Having an ongoing IIR with Shire does not preclude an investigator from submitting another proposal. Please note however that issues of non-compliance or non-conformance to the requirements of the IIR study agreement for the ongoing study may preclude you from funding until any issues are resolved.

How will I know if my proposal was received?

Email notifications will only be sent to the registered user account throughout the process. Email notifications include acknowledgement of receipt of proposal, proposal decisions of approval or decline by the review committee; and to request periodic study updates for previously approved studies. Once proposals are submitted, you may also log onto the system to view the status of your requests directly.

What if I do not receive e-mail notifications?

Check SPAM and/or Junk e-mail folders. Once located right-click on the e-mail and select the option under "Junk E-mail" to "Add Senders Domain to Safe Senders list."

Alternatively, you can manually add IIRSupport@shire.com to the safe senders list in your email account. If using Outlook, complete the following steps to add as a safe sender:

- Click on Actions, then locate the "Junk E-mail Options"
- Click on the tab for "Safe Senders"
- Click "Add", type in IIRSupport@shire.com and click "OK"

IIR Review and Decision

What is the IIR review process and cycle?

The investigator initiated research committee reviews each proposal and bases its decision on the scientific merit, alignment with Shire's strategy and safety, legal, ethical and budgetary considerations.

Please refer to <https://www.shire.com/research-and-development/investigator-initiated-research/review-cycle> for details regarding Shire's IIR Review Cycle.

Does previous support of my research by Shire guarantee future support?

No, each request submitted to Shire will be evaluated based on its individual merit, as well as the amount of overall funding still available in a particular calendar year. Please do not consider any request approved until you receive written confirmation from IIRsupport@shire.com and all necessary parties have signed the applicable written

agreement.

Who can assist me with the application process or keep me informed of the status?

The Shire IIR Team can assist you with the application process and provide status updates upon request. Questions can be sent to IIRSupport@shire.com.

Managing Approved IIR studies

How long does it take to execute an agreement?

Execution of an IIR agreement takes a minimum of 6 weeks and up to 3 months on average, depending on the complexity of the negotiations and the Institutional requirements. Please take this into account when planning timelines of your study.

What documents does Shire require prior to the start of my study?

After approval, but prior to study start, Shire must receive the following documents:

- A fully executed IIR agreement
- Institutional Review Board (IRB)/Ethics Committee (EC) Approval Documentation (IRB/EC approval letter, IRB/EC approved study protocol and IRB/EC approved informed consent form, as applicable) or IRB/EC waiver documentation
- Documentation of IND/CTA or an exemption, if applicable
- DEA223 (applicable only in the US for studies requiring controlled substance)
- IACUC approval (applicable to animal studies)

How long will it take to receive product for my study, if applicable?

Depending on the product(s) required for the study, it can take a minimum of **two weeks to six months** to receive the first shipment after contract execution. Shire will work closely with you to relay any supply related issues that may arise post IIR grant approval.

Study drug cannot be ordered until the IIR agreement is fully signed and EC/IRB, IND or CTA approval/exemption documentation has been received by Shire.

How are IIR payments managed?

IIR payments will be managed per the IIR agreement. It is the responsibility of the Institution to provide documentation to Shire of the completed milestones per the agreement.

How should study protocol changes be handled?

Study protocol changes must be submitted to Shire when there is a significant change in the design and/or implementation of the study.

If it is determined that Shire no longer wishes to support the study based on the protocol changes, Shire may choose to terminate the study in accordance with the conditions of the IIR study agreement.

Please do not submit a new IIR proposal as an amendment or a request for an IIR Amendment as new submission.

Please contact IIRsupport@shire.com with any questions.

How do I request additional funding for an ongoing study?

Requests for additional funding will be considered on a case-by-case basis, but approval is not guaranteed. Please refer to "How are Study Protocol Changes handled?" listed above.

Additional funding requests will be reviewed by the investigator initiated review committee.

REMINDER: Please do not submit a new IIR proposal as an amendment or a request for an IIR Amendment as new submission.

Please contact IIRsupport@shire.com with any questions.

What is the Study Update Report?

The Study Update Report is used to provide information to Shire on the progress of the study. In accordance with the Research Agreement, a Study Update Report must be submitted on a regular basis throughout the duration of the study. Study updates must be submitted online through the system and are required at least quarterly.

Required information includes:

- Study Enrollment information, if subjects are being enrolled:
 - Number of subjects screened
 - Number of subjects enrolled
 - Number of subjects completed
 - Number of subjects terminated
- Milestone Information
- Confirm the completed milestone(s)
- Adjust projected milestone dates as needed
- Drug Supply Information(if applicable)
- Request additional drug supply and include type and quantity

What is the Final Study Report?

The Final Study Report is a detailed summary of the study results and study conclusions. Shire requires that a final study report be submitted before the final milestone payment may be released. The Final Study Report must be submitted online through the IIR management system.

Can my contract be in my local language, or must it be in English?

Although an English version of the contract is required, an additional version in your local language can be executed.

What are the expectations with regards to publishing IIR study results?

The expected result of any Shire supported IIR study is the publication of new or confirmatory scientific and medical information.

Shire encourages investigators to exercise best efforts to publish the results of the IIR studies. Shire support of IIR studies, whether through funding, scientific advice, technical assistance and other support, must be fully and accurately disclosed in any publication or presentation of the research. Any public presentation or disclosure of study results must be reviewed by Shire prior to publication or presentation per the IIR agreement

What is Open Access?

Shire is committed to transparent dissemination of all scientific, technical and medical manuscripts generated from Shire-funded research. Therefore, for contracts initiated after January 1 2018, Shire will require the submission of all Shire-funded research manuscripts to journals that offer public availability via Open Access (including publisher platforms/repositories and self-archiving). Open Access refers to the free at point of access, online availability of published research output with rights of re-use according to users license.

Can I write about my IIR in my institution's internal newsletter?

Any public presentation or disclosure of study results must be reviewed by Shire prior to publication or presentation. Please review your contract for specific requirements regarding publication and publicity.

If you have any additional questions or would like more information regarding Shire's IIR grant submission, review and approval process, please see the more detailed IIR Guide on the portal home page (<https://ist.shiresupport.com/Shire-IIS-PROD/>) or contact us at IIRsupport@shire.com.

IIR Close-Out

How is the study close-out managed?

Once an IIR study has been completed, a final study report must be submitted to Shire's system.

All funds provided by Shire in support of the study must be reconciled. Any unused Shire products that remain at the conclusion of the study must be destroyed per the Institution's policy with the written evidence of the destruction forwarded to Shire. When the final study report has been reviewed and approved, a final invoice can be submitted for payment.

Shire IIR Team Contact Information

If you have any additional questions or would like more information regarding Shire's IIR grant submission, review and approval process, please see the more detailed IIR Guide on the portal home page (<https://ist.shiresupport.com/Shire-IIS-PROD/>) or contact us at:

Email: IIRsupport@shire.com

Webpage: <https://ist.shiresupport.com/Shire-IIS-PROD/>

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