ISR Reference Guide

Instructions and guidelines for submitting a proposal for investigator sponsored research (ISR) and conducting ISR

BAUDAX BIO®

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ISR Purpose and Mission

Baudax Bio is dedicated to supporting Investigator Sponsored Research (ISR) that advances scientific or clinical knowledge. Baudax Bio supports ISR through grants providing financial or in-kind support. ISR may be one of the following types of clinical, nonclinical, or preclinical activities: interventional, noninterventional, retrospective, prospective, epidemiological, outcomes, or screening/diagnostic.

At Baudax Bio, the ISR program is dedicated to supporting informative research that addresses meaningful clinical objectives.

Who Is Eligible?

Qualified clinicians and researchers within the United States can apply to Baudax Bio for research support. Qualifications are dependent on the type of research proposed and should be supported by a current curriculum vitae or biography.

How to Request Support

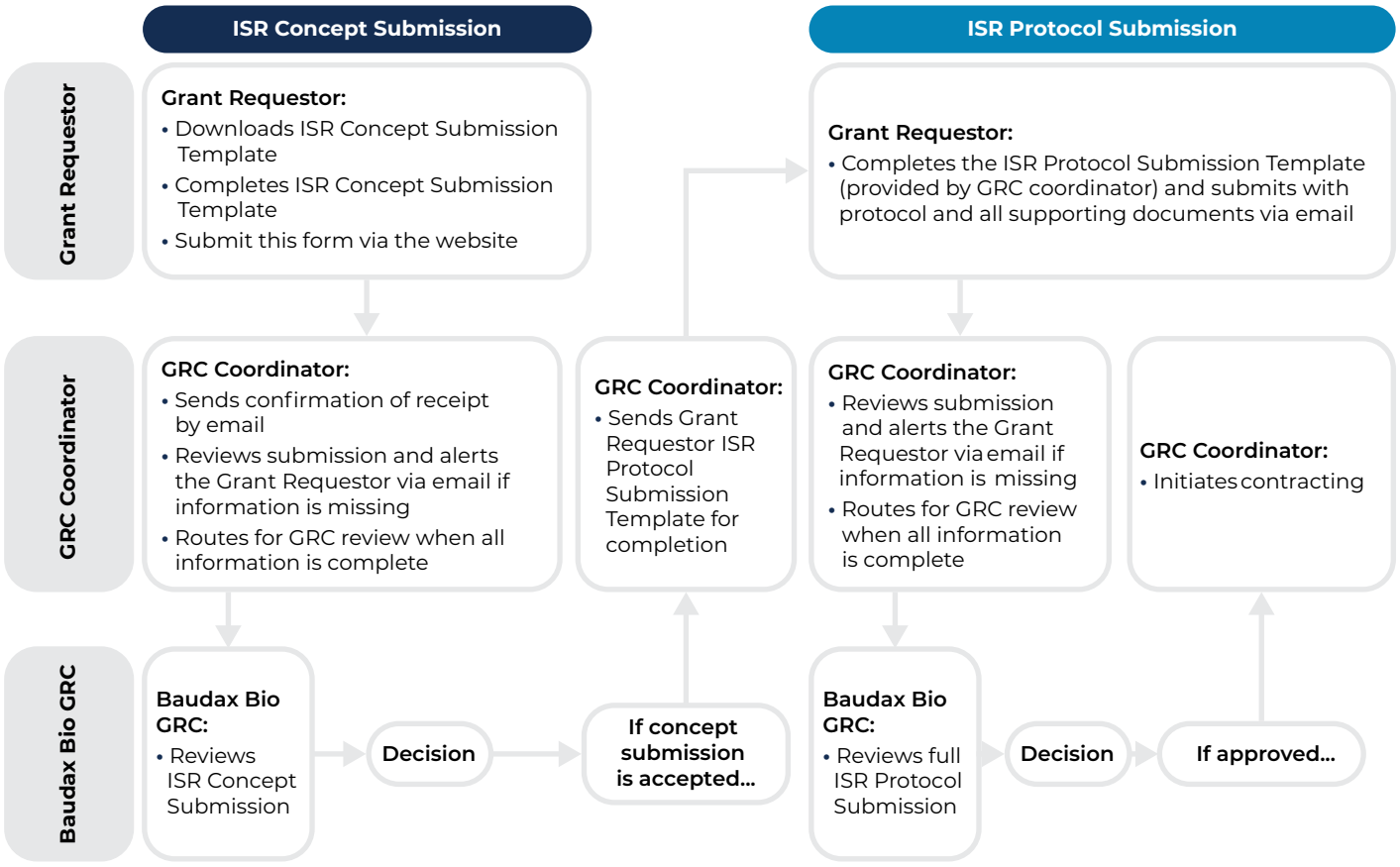
Individuals, entities, and organizations (collectively, "Grant Requestor") interested in requesting support from the Baudax Bio ISR program must first submit a concept proposal and estimated budget. The concept proposal will be reviewed by the Grant Review Committee (GRC), a multidisciplinary team at Baudax Bio.

Baudax Bio will acknowledge receipt of all ISR submissions and strive to review proposals in a timely manner. Formal notification on the status of a proposal will be sent once a decision is reached.

If a concept proposal is accepted by the GRC, the Grant Requestor will be asked to complete the ISR Protocol Submission Template and submit it along with the full protocol and a detailed budget for review.
A submission must be complete for the request to be considered.

The Baudax Bio GRC will approve only select proposals and provides no guarantee that any single proposal will receive support.

Submission Process Flow



Please send any questions regarding the submission process to ISRSupport@baudaxbio.com.

ISR Concept Proposal

A concept proposal must contain sufficient information for Baudax Bio to determine interest in receiving a full proposal with protocol. All fields should be completed in their entirety, including as much specific information as possible.

How to Submit a Concept Proposal

Step 1

Download the [ISR Concept Submission Template]

Step 2

Complete the **ISR Concept Submission Template**, including:

- Primary investigator information, including a complete CV or biography
- Clinical site information
- Sub-investigator information
- Research coordinator information
- Concept overview
  - Include investigational new drug (IND) exemption or IND submission planned
- Validated metrics of interest planned
- High-level timeline
- Investigational medicinal product (IMP) requested
- Proposed publication plan (plan for open-source publication)
- Estimated budget

Step 3

Submit the completed **ISR Concept Submission Template** via the Baudax Bio ISR webpage at https://www.baudaxbio.com/rd/investigator-sponsored-research/submission-form

- All concept proposals will be reviewed by the Baudax Bio GRC

Following receipt of a concept proposal, Baudax Bio can ask for clarification from the Grant Requestor but cannot request specific changes to the study design. Design of the study should be predominantly determined by the requestor and largely independent from Baudax Bio.

Notification of the GRC decision will be sent by email. If a concept proposal is rejected, Baudax Bio will not provide detailed feedback regarding the reasons for rejection or updates required for approval.

ISR Protocol Submission

If the concept proposal is accepted, the notification email will include the ISR Protocol Submission Template for completion along with deadlines for submission.

Please note that approval of a concept proposal does not guarantee approval of an ISR protocol submission.

How to Submit the ISR Protocol Submission Template and Full Protocol for Review

Step 1

Comply with current guidelines

- The protocol must follow the International Conference on Harmonization (ICH) E6 Good Clinical Practice (GCP) recommendations (https://www.fda.gov/media/93884/download) for protocol content

Step 2

Complete the **ISR Protocol Submission Template**, which will be sent with the concept acceptance. Include the following elements:

- Grant Requestor contact details
  - Name, address, and qualifications of the Grant Requestor(s) seeking the funds or IMP along with a complete CV or biography.
  - Name, address, and federal tax identification number of the institution(s) with which the research is affiliated
  - Copies of current relevant licenses
- Proposed research protocol that describes the study objective(s), design, methodology, any statistical considerations, timelines, and organization of the study
- Study design
  - Primary and secondary endpoints
  - Description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled)
  - Description of methods and overall study flow
- Subject eligibility
  - Clearly defined inclusion and exclusion criteria
  - Withdrawal and discontinuation conditions
- Study treatment
  - Description of study treatments and other interventions, including timing of dosing, duration of treatment, and use of any other defined medications
  - Storage of medication(s)
  - Blinding details (if appropriate)
  - Randomization details (if appropriate)
- Data capture and analysis
  - Roles and responsibilities
  - Methods of data capture
  - Demographic data
  - Efficacy assessments, including details regarding how and when assessments are to be performed
  - Safety assessments, including appropriate safety measurements and how and when they are to be performed
    - Assessment of adverse events and serious adverse events including intensity, causality, and reporting conditions
- Statistics
  - Sample size determination
  - Definition of subject populations (safety, intent to treat, modified intent to treat)
  - Description of statistical methods, including a detailed statistical analysis plan
- Study administration
  - Regulatory and ethics considerations
  - Study monitoring
  - Quality assurance
- Publication plan, including abstract(s), meeting presentation(s), manuscript, and planned journal (plan for open access publication), along with posting to a public web site such as www.ClinicalTrials.gov
- Full budget (itemized and detailed; see STEP 3)
- References (as appropriate)
- Appendices (as appropriate)
  - Overview of study schedule/procedures
  - Study-specific assessment tools/scales
  - Treatment protocol details

Step 3

Itemize all expected study-related expenses. The following are examples of costs that may be relevant when calculating an itemized budget:

- Subject-related costs
- Study-related personnel costs
- Contract research organization costs
- Diagnostic fees/services
- Data management expenses
- Institutional review board (IRB) review fees
- Equipment and supply expenses
- Animal-related costs (if appropriate)
- Publication costs

Baudax Bio research grants shall not be:

- Used in any way to defray a recipient's ordinary operating expenses (i.e., expenses of activities that the recipient is already required to perform or customarily performs) or to support research that has already occurred
- Made in the form of company stock, stock options, or other forms of share-based compensation
- Provided with the intent of directly or indirectly, or implicitly or explicitly influencing or encouraging the recipient to prescribe, purchase, recommend, sell, or arrange for or recommend the prescribing, purchasing, or sale of any Baudax Bio product or as a reward for any such past behavior
- Used to support consulting or other services to Baudax Bio

Step 4

Email the completed ISR Protocol Submission Template, full protocol, and budget documents to Baudax Bio at ISRSupport@BaudaxBio.com for evaluation

- If the ISR protocol submission is accepted, the Research Grant Agreement will clearly define the terms of the research as well as the roles and responsibilities of the Grant Requestor

Grant Requestor Responsibilities

The Grant Requestor is responsible for making all necessary regulatory submissions, including the submission of an IND application or exemption (if necessary) as well as obtaining IRB review and providing required interval updates. The Grant Requestor is also responsible for:

- Fully reviewing and ensuring the accuracy and completeness of all information provided by Baudax Bio regarding requirements associated with the proposal and protocol submission for the approval of an ISR
- Public registration of the study on a public website such as www.ClinicalTrials.gov
- Conducting and executing the trial in adherence with the approved proposal and finalized ISR Research Grant Agreement with Baudax Bio, with limited contact with Baudax Bio
- Study design, operational conduct, administration, and adherence to all regulatory and ethics requirements, including but not limited to:
  - Good Clinical Practice (GCP): https://www.fda.gov/media/93884/download
  - Good Pharmacovigilance Practices (GVP): https://www.fda.gov/media/71546/download
  - Safety Reporting Requirements: https://www.fda.gov/media/79394/download
  - Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators: https://www.fda.gov/media/92604/download
- Selecting and contracting with any service providers needed to operationalize the study
- Data dissemination, including timely publication in a peer-reviewed journal and presentation, as appropriate, at a scientific congress as consistent with the terms of the Research Grant Agreement
- Development of and adherence to a mutually agreed upon timeline, including periodic and as-required study updates to Baudax Bio

Status Reporting

Grant Requestors who receive Baudax Bio support must agree to periodic and as-required monthly study updates. The Grant Requestors shall provide their study updates on the first of each month using the ISR Status Update form. These updates may include (but are not limited to):

- Submission of the study description that is required to be posted on a public website (e.g., www.ClinicalTrials.gov) to Baudax Bio prior to public disclosure
- Details such as patient enrollment or number of animals treated, etc.
- Any amendments to the original protocol
- Proof of approval of the study (and any changes requested or required) by local or national regulatory authorities and ethics committees
- Adverse events and serious adverse events
  - It is the Grant Requestor's responsibility to report adverse events to the appropriate regulatory authorities and to notify Baudax Bio as specified in the Research Grant Agreement
- Plans to publish and/or present interim and/or final study results
- Notification of study completion

Regulatory, IRB, and Safety Reporting

Grant Requestors who receive Baudax Bio support must conduct their research according to ICH GCP provisions (https://www.fda.gov/media/93884/download), if applicable, and comply with all national and local rules, regulations, and safety reporting obligations.

This includes (but is not limited to) activities such as:

- Securing country-specific regulatory approvals, if required
- Applying for and obtaining ethics committee or IRB approval
- Reporting required data to local authorities
- Reporting adverse events to the FDA and/or other applicable regulatory or local authorities

Study Registration, Publication, and Reporting

Baudax Bio requires Grant Requestors who receive Baudax Bio support to post approved information about their clinical studies on a public clinical trials website, such as www.ClinicalTrials.gov.

Financial Disclosure by Baudax Bio

Baudax Bio is committed to meeting its federal and state statutory transparency requirements and accordingly may disclose the funding associated with an ISR.

For more information, please visit BaudaxBio.com.

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