

# REQUEST FOR PROPOSALS

## My Seizure Gauge Initiative

*Bringing Big Data to Personalized Seizure Risk Assessment*

The Epilepsy Innovation Institute (Ei<sup>2</sup>) is pleased to announce a Request for Proposals for the My Seizure Gauge initiative pairing longitudinal intracranial EEG recordings with a host of peripheral measurements (such as biosensors, digital markers, passive measurements, etc.) to identify new relationships between brain state and non-invasive or minimally invasive read-outs. A successful team will be composed of clinicians who can recruit participants with existing intracranial devices implanted, data scientists and device interoperability experts who can ensure successful data integration, and researchers who can propose different parameters to measure and analyze. Ei<sup>2</sup> plans to fund at least \$3 million to a team over a three-year period.

Recognizing that not all organization(s)/individual(s) interested in participating have existing partnerships that would ensure a successful full grant application, all interested parties are encouraged to submit an LOI by December 22nd addressing which assets the individual(s)/organization(s) could contribute to the project. Those with accepted LOIs will be invited to a February 21<sup>st</sup> workshop in San Francisco, California where there will be opportunities to find partners prior to the full grant application and have discussions on key decision criteria for a successful grant. Note that pre-formed teams may also submit an LOI, and if selected, attend the workshop. Please see [Letter of Intent section under Applicant Instructions](#) for more details. Full grant applications will be due on May 11<sup>th</sup>, 2018.

Our overall goal is to collect prospective data from a cohort of individuals who have had intracranial EEG devices implanted. The ideal application will outline a recruitment process for individuals with ambulatory intracranial EEG recordings, propose rigorous methodology to measure a myriad of additional factors, and then mine the data for new clues about what happens in the body in the days, hours and minutes before a seizure. Insights from this study can then be used to design less-invasive approaches to a future seizure gauge device for forecasting seizures.

### TABLE OF CONTENTS

Introduction.....	2
Objectives and Strategic Areas of Interest .....	3
The Time is Right.....	3
Team Science Award.....	4
Applicant Eligibility .....	4
Application Instructions:.....	5
Letter of Intent .....	5

February Workshop .....6

Full-length Application.....6

Timeline .....9

Review Mechanism.....9

Award Administration.....9

    Award Letter .....9

    Approvals.....10

    Multi-Institutional Projects.....10

    Funding .....10

    Annual Meeting .....10

Frequently Asked Questions.....10

    Eligibility.....10

    Application Components .....11

    Additional Information and Contacts .....12

## INTRODUCTION

The Epilepsy Innovation Institute (Ei<sup>2</sup>) is a research program of the Epilepsy Foundation, a 501(c)3 nonprofit whose mission is to lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, fund cures and save lives.

In 2016, Ei<sup>2</sup> released an online survey asking the community what aspects of epilepsy impact them the most. Over one thousand individuals responded from across the United States and abroad. An overwhelming majority of respondents, regardless of seizure frequency and type, selected unpredictability of seizures as a top issue. Many wrote about the fear of not knowing *when* a seizure will start and not knowing *what* triggers the seizure onset.

In response to this input, the Epilepsy Foundation, through Ei<sup>2</sup>, launched the My Seizure Gauge challenge. The moonshot goal is to create an individualized seizure gauge that will allow a person with epilepsy to monitor the likelihood of a seizure on a daily basis. In the first phase on the challenge, the goal is to identify and better understand the changes in the body that may precede the onset of a seizure, at a time course that may be hours or days before the clinical (observable) seizure. **This project will lay the groundwork to:**

- Know when a seizure is likely or unlikely – empowering people to achieve better control
- Prevent or stop the progress of a seizure before it starts (tailoring the therapy to the start of seizure onset)
- Personalize dosing of medication and device stimulation (fine-tune it to when it is needed) to reduce treatment side-effects

- Incorporate new non-EEG based drug screening tests in existing and new animal research models to improve a drug's effectiveness for preventing seizures
- Identify and explain why certain situations, such as stress, may trigger a seizure
- Better understand the biological profiles of epilepsy syndromes, which in turn could improve diagnosis and address WHY seizures occur in an individual
- Suggest novel therapeutic targets that could be developed into new therapies for epilepsy
- Provide new insights into less invasive wearable EEG technology.

Prior to releasing this RFP, Ei<sup>2</sup> hosted an innovation workshop to assess the current state of the science in seizure forecasting and seizure risk assessment. [For more information on the outcomes of the workshop, please download Workshop Notes in templates section of ProposalCentral.](#)

## OBJECTIVES AND STRATEGIC AREAS OF INTEREST

The objective of this RFP is to support an implementation plan for a multidisciplinary team to follow a cohort of individuals with ambulatory intracranial EEG implants and pair these measurements with other additional parameters (such as biosensors, digital markers, passive measurements, etc.). The goal is to identify and understand the impact that changes in the body and environment have preceding a seizure on a timescale of minutes to hours to days prior to the event. The cohort will be followed for over a year, and this data will feed into a common data collection platform. This is a longitudinal, long-term effort to transform the understanding of factors contributing to seizure susceptibility and to create future personalized algorithms that could forecast daily seizure probability.

The intent of the My Seizure Gauge Challenge is for the originators of the data to be allowed to commercialize their insights. However, Ei<sup>2</sup> will have non-exclusive rights to license the data for research purposes to glean new insights into seizure forecasting and our understanding of epilepsy.

## THE TIME IS RIGHT

The ability to accurately predict seizures has been sought for decades. Why is now the right time? Outlined below are factors that have changed over the last decade that could enhance chances for success.

1. Previously, only short-term intracranial EEG data (typically up to 1 week) was available for analysis from pre-surgical monitoring units (Mormann, Andrzejak, Elger, & Lehnertz, 2007). The short-term recordings are too limited a time span for interictal (between seizures) and ictal (seizure) data to build patient-specific models for seizure likelihood. There are now over a thousand individuals who have ambulatory intracranial EEG systems, either through the FDA approved Neuropace RNS system or through the Activa PC system by Medtronic, in clinical trials. This allows access to real-time longitudinal data (on a timescale of years) of EEG recordings. Obtaining EEG ensures that real world seizure events can be validated against the current EEG gold standard in this patient population.

2. With the advances in bioengineering and biosensors, capability exists to acquire noninvasive multimodal data that allow identification of potential lead candidate signals that inform about seizure probability to circle back and test. Indeed, optical measures of motion and stress and sweat sensing technologies have advanced rapidly in just the past 5 years.
3. Large-scale machine learning capabilities have advanced. Machine learning is not the answer for all problems, but it works well with unstructured data. However, for such an approach to be meaningful, subject matter expertise is critical to ensure accurate classifications of the data and interpretable results. For example, mathematical modeling of electrophysiological signatures of seizures from flies to humans is evolutionarily conserved. A recent group classified these seizure signature profiles into 16 distinct categories (Jirsa et al., 2014). Using this new taxonomy may spur different insights into seizure mechanism that could help interpret the data findings and find correlations in body chemistry associated with these different seizure classifications.

## TEAM SCIENCE AWARD

This award is designed to foster collaborative research amongst researchers with complementary expertise and capabilities, who will work together to advance our understanding in seizure risk assessment. Ei<sup>2</sup> expects to provide at least \$3 million over three years to multidisciplinary teams of two or more established Principal Investigators (PIs).

Teams may consist of investigators from the same institution, different institutions, may be public/private partnerships and may be international. A designated Administrative PI is responsible for administrative leadership in ensuring all documents are submitted (see Application instructions). All PIs on the team share authority for scientific leadership. A representative of Ei<sup>2</sup> will also be part of the selected winning team.

This award has a collaborative and multidisciplinary emphasis, involving meaningful collaboration between participants. **Applications therefore must include a description of the nature of and rationale for the proposed collaboration, the specific role of all PIs, and synergistic opportunities.**

Note that a successful full grant application will need a team with expertise and capacity to address the following:

- Recruitment of individuals with ambulatory intracranial EEG devices implanted
- Cross-talk (device interoperability) between different sensing modalities / devices proposed
- Data platform capabilities on how data is housed, integrated, stored, and archived
- Why the modalities proposed would provide new insights into seizure forecasting

## APPLICANT ELIGIBILITY

PIs must hold a full-time faculty or industry appointment at the level of Assistant Professor (or equivalent) or above at an academic, non-profit research institution, or industry organization whose primary mission includes medical research within or outside the United States. PIs must be able to show

clear evidence of an independent research program. Fellows or those in other training or research support positions are encouraged to be part of the team. Investigators need not be specifically trained in the field of epilepsy or have any documented experience with epilepsy research. However, researchers who are new to epilepsy will need to ensure that there is an epilepsy research expert on their team during the formative stages of the research plan. If there are any questions about eligibility, please contact Ei<sup>2</sup> before submitting an application. Contact information appears at the end of this RFP. Applications from PIs who do not meet the eligibility criteria will not be reviewed.

## APPLICATION INSTRUCTIONS:

There will be a two-stage peer-review application process:

1. Letters of Intent (LOIs) are due by 5:00 PM Eastern Time on Friday, December 22<sup>nd</sup>, 2017.
2. Epilepsy Foundation will select one or more LOIs to advance to full review. These applicants will be invited to a Feb 21<sup>st</sup> Workshop in San Francisco, CA. Following the workshop, full-length proposals will be due by 5:00 PM Eastern Time on May 11<sup>th</sup>, 2018.

All applications are due by 5:00 PM Eastern Time on the dates specified above. LOIs and proposals received after the applicable deadline will not be considered.

The Epilepsy Foundation utilizes the [proposalCENTRAL](#) online application tool and the document templates and requirements therein. Please carefully follow the instructions in [proposalCENTRAL](#) and below. Applications include the following steps and components.

## LETTER OF INTENT

All applicants must submit a LOI to the Epilepsy Foundation prior to submission of a full proposal. Please carefully follow the instructions in [proposalCENTRAL](#). The LOI application consists of the following components:

1. **Title Page:** Enter the project title. (Title length cannot exceed 75 characters)
2. **Applicant/PI Information:** For Team applications, identify one PI for administrative purposes of grant submission. This is the Applicant.
3. **Organization/Institution Information:** This is the Administrative PI's institution.
4. **Key Personnel Information:** Identify other PIs on the team. All PIs share authority for project leadership.

5. **LOI:** 2-page maximum that must be formatted in Arial 11 point or Times New Roman 12-point font with no less than ½ inch margins. Components of the LOI include:

(a) a description of how the team/individual/organization can contribute to the project, and  
(b) If in a team, the nature of and rationale for the proposed collaboration, the specific role of each participant, and synergistic opportunities, or if not yet in a team, how the individual/organization envisions working in a team.

(c) Depending on the individual(s)/organization(s) applying, one would also need to address:

- If clinician recruiter – estimated numbers and strategy for recruitment
- If data platform suggested – HIPAA compliance, prior experience with how data is stored, housed, integrated, archived
- If device interoperability expert – strategy to ensure time synchrony, device cross-talk
- If biosensor/digital marker – what new insights could this parameter shed in epilepsy, how would data be collected, and would there be access to raw data to input into a data collection platform
- If an industry partner, a description of what they could contribute and how they envision the partnership with Ei<sup>2</sup> working

(d) Description of how the methodology and results might lead to future development of a non-invasive Seizure Gauge.

Letters exceeding the 2-page limit will not be considered.

## FEBRUARY WORKSHOP

The applicants associated with the LOIs that are selected to advance will be invited to a February 21<sup>st</sup> Workshop in San Francisco, CA. Travel to the workshop will be covered by the Foundation. The workshop will also consist of other stakeholders not represented in the LOI applicant pool. The purpose of the workshop is to provide an opportunity for partnerships and roadmap potential inflection points and key go/no-go criteria for the grant proposals. LOI applicants can either assemble their own team or build upon the partnerships developed at workshop or elsewhere prior to submitting a full-length application.

## FULL-LENGTH APPLICATION

Full-length applications will be invited from meritorious LOIs selected by the Epilepsy Foundation Ei<sup>2</sup> review committee. The submissions will be open following the February workshop.

Please carefully follow the instructions in proposalCENTRAL and below. Applications include the following steps and components.

1. **Title Page:** Enter the project title.
2. **Templates and Instructions:** Download RFP and templates.
3. **Enable Other Users to Access this Proposal:** Allow others (e.g., institutional administrators or collaborators) to view, edit, or submit your proposal.
4. **Applicant/PI:** Key information about the applicant PI. This must be the Administrative PI on team science applications.
5. **Organization/Institution:** Key information about the Applicant/PI's institution, including name and email address of the signing official who, in addition to the PI, will be contacted if the award is selected for funding.
6. **Key Personnel:** List and provide contact information for key persons. Include all PIs on the proposal as well as any additional key personnel.
7. **Abstracts and Keywords:** Provide a lay audience friendly abstract and a technical abstract (2,000 characters maximum each) and key words. Please note: the lay abstract will become public if the award is selected for funding; therefore, it should not contain any proprietary information.
8. **Budget Period Detail:** Enter budget detail for each award period requested. For proposals involving multiple institutions, please include a total amount requested for each institution in the designated spaces provided. Epilepsy Foundation will not support indirect costs, overhead costs, or other similar institutional levies in excess of 10% of the total award amount. Fringe benefits for personnel salaries are allowable. Each performance site must submit a separate budget using the Ei<sup>2</sup> Budget Form. Budgets must be signed by an authorized institution official and uploaded into the web-based submission system along with the compliance form and this proposal narrative.
9. **Budget Summary and Justification:** A description of why the attached budget is appropriate for the proposed work. Be sure to include personnel responsibilities and effort commitments. Equipment is generally not supported but may be on occasion if well justified by the needs of the project. Project periods are expected to be over the course of three years. Each performance site must submit separate budgets using the Ei<sup>2</sup> Budget Form.

10. **Organizational Assurances:** Ensure Compliance with Human Subjects and Animal Care Assurance as applicable.

11. **Upload Attachments:** Upload the following:

- a. **Curriculum vitae for PIs and other key personnel:** Applicants may use the template provided or the NIH biosketch format.
- b. **Current and pending research support for the PIs:** Use the template provided in proposalCENTRAL, which includes a statement of overlap. Any overlap of current or pending support with the Epilepsy Foundation proposal must be described and explained.
- c. **Project description:** Must be formatted in Arial 11 point or Times New Roman 12 point font with no less than ½ inch margins. 10 pages maximum, inclusive of the following:
  - i. Abstract
  - ii. Proposed Solution
  - iii. Alternative Approaches
  - iv. Work Plan and Aims
  - v. Team
  - vi. Managing Challenges
  - vii. Explanation of how the project meets the requirements of the My Seizure Gauge Challenge including how the insights learn could be extended to less invasive approaches for a Seizure Gauge in the future
  - viii. Implementation Pathway

Descriptions exceeding the 10-page limit will not be considered.

d. **Cited references:** A list of up to 20 references (maximum) supporting the project description is allowed, in addition to the 5-page project description.

e. **IRB protocol (or international equivalent):** We recognize that the IRB approval (or international equivalent) may not have been granted by the time of the grant submission, however we request that a proposal be submitted for review by the time of the full grant application, and that this protocol is uploaded to the grant review. If the IRB application (or international equivalent) is approved, please list the number.

f. **For multi-institutional proposals:** Attach a letter from the Administrative PI's institution confirming that if the award is made, the institution will execute the necessary sub-award agreements within 30 days of execution of the award agreement between Epilepsy Foundation and the applicant institution and will transfer funds from their institution to the collaborating institution(s).

12. **Validate:** Check for any missing required information.

13. **Signature pages:** Print the signature page, which must be signed by the PI and the institution's signing official, and uploaded as part of the application package.

14. **Submit:** Please note that no proposals will be able to be submitted past the deadline. Technical support for the on-line application system is not available after 5:00 PM Eastern Time.

## TIMELINE

- **December 22<sup>nd</sup>, 2017:** Letters of Intent are due by 5:00 pm Eastern Time.
- **Mid-January, 2018:** Teams from meritorious LOIs are invited to attend the Feb 21<sup>st</sup> workshop in San Francisco, California
- **Feb 21<sup>st</sup> workshop:** Selected applicants from meritorious LOIs will convene to discuss logistics of grant proposal and potential for partnerships.
- **May 11<sup>th</sup>, 2018:** Full-length proposals are due by 5:00 PM Eastern Time
- **June, 2018:** peer and organizational review
- **July/Early August, 2018:** Awardees notified (Epilepsy Foundation may adjust date without notice to applicants)
- **September, 2018:** Projects commence

## REVIEW MECHANISM

All proposals will undergo rigorous peer review by the Epilepsy Foundation, comprised of experts in Epilepsy and diverse areas of data science, multimodal integration, and precision medicine. Applications will be scored based on approach, innovation, investigator team & environment. Specifically, the quality of the science, strength of the team, uniqueness and thoroughness of the approach and value relative to the budget will be considered.

The Epilepsy Foundation will provide reviewer critiques or evaluations to applicants through proposalCENTRAL. Depending on peer review and Ei<sup>2</sup> program priorities, the Epilepsy Foundation may work with applicants to modify the submitted work plan and/or budget.

## AWARD ADMINISTRATION

### AWARD LETTER

Upon acceptance of an award, the PI and his/her employing Institution will be required to sign an Award Letter indicating acceptance of Epilepsy Foundation Award Terms and Conditions within 30 days. The Epilepsy Foundation must be notified in advance and approve of any significant changes in research

objectives, key personnel, or budget both at the time of the award and throughout the term of the award. This includes moves of key personnel between institutions.

## APPROVALS

The Epilepsy Foundation requires certification through proposalCENTRAL of compliance with Human Subjects and Animal Care Assurance as applicable. In cases where ethical/regulatory approval is required to perform the work, such approvals will be required before initial payments are made.

## MULTI-INSTITUTIONAL PROJECTS

For projects including key personnel at other institutions, the PI must verify in advance that funds can be transferred from his/her institution to the collaborating institution. This requirement can be met by attaching a letter from the PI's sponsored programs office stating a commitment to comply with this requirement. Sub-award agreements between collaborating institutions must be executed within 30 days of the Epilepsy Foundation's execution of the award agreement with the applicant institution, and will be subject to the Epilepsy Foundation Award Terms and Conditions.

## FUNDING

For all proposals, the level and duration of funding may be adjusted by the Epilepsy Foundation as appropriate for the scope of the proposal and the funds available. Partial funding will also be considered to obtain proof-of-principle data in support of innovative ideas with transformative potential. The Epilepsy Foundation will not provide more than 10% of the total award amount for indirect costs, overhead costs, or other similar institutional charges. Full-term funding will be contingent upon review of annual progress reports and other oversight activities conducted by the Epilepsy Foundation. Multi-year support is not automatic for any Epilepsy Foundation award and is conditioned on submission of complete and accurate progress reports and demonstrated progress on the funded proposal.

## ANNUAL MEETING

PIs whose projects are selected for funding are expected to attend the annual Ei<sup>2</sup> meeting, at which they will present research findings made under their awards to an advisory group. The Epilepsy Foundation will cover reasonable travel costs related to participation in these meetings.

## FREQUENTLY ASKED QUESTIONS

### ELIGIBILITY

**Q: Must PIs have an academic faculty appointment? Is this a hard-and-fast rule?**

**A:** PIs must have a full-time appointment at an academic, non-profit research institution or biomedical-focused industry organization at the level of Assistant Professor (or equivalent) or above; however,

while a tenure-track is preferred, it is not required. Evidence of independent investigator status and an environment conducive and supportive of translational research is required. If there is any doubt or question about a PI's eligibility, please contact Ei<sup>2</sup> (contacts provided below) before an application is submitted. Applications from PIs who do not fit the eligibility criteria will not be reviewed.

**Q: Does Ei<sup>2</sup> fund investigators and institutions outside of the United States?**

**A:** Yes, investigators at institutions outside of the United States are eligible. PIs must be at the level of Assistant Professor or equivalent. Academic appointments of institutions outside of the US can differ from those traditionally found in the US. Contact Ei<sup>2</sup> if there are any questions about eligibility prior to submitting a proposal.

## APPLICATION COMPONENTS

**Q: How are LOIs submitted? Do I need to send a hard copy?**

**A:** All LOIs must be submitted electronically via proposalCENTRAL. The signature page should be signed and a scanned PDF copy be uploaded as part of the application in proposalCENTRAL. Hard copies will not be accepted.

**Q: If I am invited to submit a full proposal, do I have to go to the February workshop?**

**A:** Yes. The February 21<sup>st</sup> workshop will be hosted in San Francisco, CA. All travel to the workshop will be covered by the Epilepsy Foundation. The goal of the workshop is to discuss key considerations for a successful grant application and to find potential partners to strengthen the full proposal application.

**Q: Do I need to partner up with other members at the February workshop to submit a full proposal?**

**A:** No. If there are other members that you find would make your grant stronger, we encourage you to facilitate other collaborations. The workshop will still be beneficial for applicants to strengthen their proposals prior to applying.

**Q: How are proposals submitted? Do I need to send a hard copy?**

**A:** All proposals must be submitted electronically via proposalCENTRAL. The signature page should be signed and a scanned PDF copy be uploaded as part of the application in proposalCENTRAL. Hard copies will not be accepted.

**Q: Does the Epilepsy Foundation require the NIH salary cap to be used when calculating salary and fringe benefit requests for the budget?**

**A:** Yes.

**Q: What needs to be included in the "current and pending support" section?**

**A:** Please submit a listing of all sponsored research support for the effort of the PI that is active or pending (submitted or awarded by a research sponsor but not yet started). Include the title of the project, research sponsor, total annual funding, start and end dates, and percent of committed

time. For each project, you must include a statement of overlap or non-overlap with the Ei<sup>2</sup> My Seizure Gauge proposal. A template is provided in proposalCENTRAL.

**Q: Is the NIH biosketch CV format acceptable for submission?**

**A:** Yes, you may use your NIH biosketch or the template provided in proposalCENTRAL.

**Q: Could the team be composed of a public/private partnership?**

**A:** Yes, the team can be a mix of industry and academic partners.

#### ADDITIONAL INFORMATION AND CONTACTS

Technical questions about the proposalCENTRAL submission system should be directed to their customer support at 800-875-2562 (Toll-free US and Canada), +1 703-964-5840 (Direct Dial International), or by email at [pcsupport@altum.com](mailto:pcsupport@altum.com).

For administrative questions regarding this RFP and eligibility, please email Liz Schreiber, Grants and Fellowships Program Manager, at [lschreiber@efa.org](mailto:lschreiber@efa.org).

For other questions regarding the My Seizure Gauge initiative, please contact Sonya Dumanis, Senior Director of Innovation, at [sdumanis@efa.org](mailto:sdumanis@efa.org).