Research Accelerator for Follicular Lymphoma - I (RAFL- I)

Synergistic Team Award (STA) Guidelines and Instructions

Effective dates:
July 1, 2024 – June 30, 2025

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Application Compliance

- It is highly recommended to access the **LLS Research Portal** at https://lls.fluxx.io and begin the application process well in advance of any deadlines. In addition, each stage of the application process (letter of intent/full application) should be completed well before the deadlines.

- No aspects of the application, except regulatory approvals, will be accepted past the deadline.

- All components of the application must be presented in the order indicated in these guidelines.

- Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. Font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself. **If character limits and font restrictions are not adhered to, or the preset margins are altered, the application may be administratively disqualified.**

- Line spacing is preset in the Word document. **Do not change this setting**. Pasting text from another document into the template may result in a change in the line spacing. Check the line spacing in the template before pasting, and if there is a change after pasting, return the line spacing to the original setting. Any modifications in line spacing, particularly if the change allows for more text to fit into the page, **may result in administrative disqualification of your application.**

- Do **not** attach documents to the application that are not specifically called for.
  The application may be administratively disqualified if this rule is violated.

- **The STA Director and/or Project Leaders** may apply to more than one grant program during an application cycle if the aims do not substantially overlap with the aims of any other application across all programs.

- All duplicate grant proposal submissions with substantially overlapping aims are subject to administrative disqualification, and such proposals will not be reviewed further or considered for funding. Contact researchprograms@lls.org with any questions about this policy or to discuss with LLS scientific staff any questions concerning potential overlap.

- Completion of several steps in the process initiates emails from the LLS Research Portal. LLS staff may also send emails during the application process. Spam filters should be monitored for these emails. Contact researchprograms@lls.org if expected emails are not received by the times indicated in these guidelines or if you have any questions not clarified in this document.

- Note that **there are two subprograms under the RAFL Research Initiative.** Please ensure that you are applying to the subprogram that best fits the goals and structure of your proposal.

About The Institute for Follicular Lymphoma Innovation

The Institute for Follicular Lymphoma Innovation (IFLI) is a global non-profit, private foundation dedicated to accelerating the development of innovative treatment options for patients with follicular lymphoma. IFLI supports cutting-edge research and technology to lead to the development and commercialization of novel therapeutics and/or biomarkers for the treatment of follicular lymphoma (FL), and to understand the biology of FL. The foundation deploys its budget across grants, project-based partnerships, and venture philanthropy investments to achieve its innovation goals. IFLI aims to promote data sharing among researchers and institutions working on different aspects of FL research, fostering collaboration, and enabling the exchange of knowledge and expertise. Learn more at i-fli.org.

About The Leukemia & Lymphoma Society, Inc.

The Leukemia & Lymphoma Society, Inc. (LLS) is a national voluntary health agency dedicated to the conquest of hematologic malignancies and relevant premalignant conditions. LLS supports research, patient aid, community service programs, advocacy, and public and professional education.

Program Description

Follicular lymphoma (FL), a type of non-Hodgkin lymphoma, is an indolent blood cancer for which there is no cure. FL patients may experience varied clinical courses. For many patients, FL will progress slowly and either not require therapy (a “watch and wait” situation) or respond well to chemoimmunotherapy. Many of these patients enjoy long survival times with no additional therapy. However, some patients either do not respond, or will relapse after a long period of remission. In its most aggressive form, some patients (3-8% within 10 years of diagnosis) will experience transformation of FL to a rapidly progressing disease (tFL) leading to mortality within a few years after transformation[i]. Therefore, better treatment strategies for long-term FL control are needed in each of these varied populations. Ultimately, the overarching goal is to achieve a cure in which FL is eradicated, and therapy can be discontinued.

To achieve this bold goal, scientists and clinicians must tap into the innovations and emerging technologies to solve three critical objectives. In this next era of FL research, we believe:

- The biology of non-responders and patients who relapse can be targeted for therapeutic effect. New technologies may elucidate the unique biology of indolent lymphomas and their tumor microenvironment (TME), pinpointing mechanistic vulnerabilities[ii].
- More durable response can be achieved. New diagnostic and monitoring strategies may optimize the sequencing of immunotherapy and precision medicine approaches[iii].
- Better methods to identify patients at risk of transformation of FL (tFL) can be developed, along with new targets and treatment regimens to reduce the burden of early mortality in tFL patients[i].
- Serendipitous observations will open new avenues of investigation.

To address these challenges and to encourage innovative research, The Leukemia & Lymphoma Society (LLS) and Institute for Follicular Lymphoma Innovation (IFLI) have joined forces in a strategic partnership called the Research Accelerator for Follicular Lymphoma (RAFL).

LLS and IFLI are jointly funding creative and ambitious research and development proposals under the RAFL program. International and US-based applicants are welcome to apply. Two funding cycles are anticipated (RAFL-I opening 2024, with funding commencing in 2025) and (RAFL-II opening in 2026, with funding commencing in 2027), with total funds of at least $20 million US dollars available for meritorious research.

Innovative projects that have the potential for high impact in the field of FL may cover discovery, translational and/or clinical research. Successful candidates will be established investigators in FL or related fields with demonstrated track-records of significant contributions. Cross-disciplinary collaboration including industry partnership is encouraged. Teams may be strengthened with investigators who bring special expertise in epigenetic or apoptotic control, computational skills, data science/AI, animal model development, neoantigen discovery and antibody treatment to the project in FL.

[i] Parry et al. DLBCL arising from indolent lymphomas: How are they different? Seminars in Hematology 2023; 60: 277-284.

[ii] Radtke et al., Multi-omic profiling of follicular lymphoma reveals changes in tissue architecture and enhanced stromal remodeling in high-risk patients. Cancer Cell 2024; 42: 444-463.

[iii] Friedberg, J. Update on follicular lymphoma. Hematological Oncology. 2023; 41(S1): 43-47.

Research Focus Areas

The development of new therapeutic options and monitoring strategies will address key unmet needs in FL. Potential areas of interest are described below.

- New Therapeutic Development – Development of new chemical entities and other therapeutic approaches is needed to address disease heterogeneity and resistance/relapse. Examples include:
  - New therapeutic modalities such as, but not limited to, BCL6 degraders, CREBBP controllers, transcriptional regulators.
  - Immunotherapy agents targeting novel antigens or leveraging the activity of other agents.
  - New therapies for transformed FL.
  - New therapeutic approaches that impact patient quality of life.

- Target Identification - Leveraging innovation in, for example, genomics, computational biology, and data science for identification of novel therapeutic targets.

- Follicular Lymphoma Biology - Research programs to identify and understand the cellular and molecular determinants of tumor heterogeneity driving FL progression, treatment resistance, and transformation. Examples include:

  - Common precursor cell – identification and demonstration by functional studies that disease and progression/recurrence are driven by a common precursor cell. Design of new therapeutic strategies to eradicate common precursor cells.
  - TME and immune biology – identification and demonstration of changes in TME that contribute to FL resistance and/or transformation.

- Biomarker Discovery and Development – Research programs to identify and validate surrogate or ancillary biomarkers for FL and tFL. Examples include:
  - biomarkers to improve diagnostic and disease progression prediction (e.g. POD 24, tFL) via patient stratification, to inform treatment selection, to allow response monitoring, and to decrease time on ineffective therapies.
  - biomarkers in non-relapsing patients to determine if functional cure is durable, complete cure.

- Monitoring and Diagnostics - Leveraging innovation in next-generation sequencing to diagnose relapse before clinical or radiological evidence, optimize treatment response and inform treatment selection. Plasma-based methods have the potential to improve monitoring and enhance patient quality of life.

- Translational tools and technologies –
  - new disease models including preclinical animal models.
  - leveraging data science/AI to drive discovery and development of new personalized medicine approaches.

RAFL- I Grant Funding Mechanisms

LLS and IFLI are activating a global call for innovative proposals with potential for high impact in the field of FL. RAFL-I will support two types of awards, Synergistic Team Awards (STA) and Translational Grants (TRL)

- **Synergistic Team Award** —This multi-investigator grant is designed to support a coordinated, focused, and significant effort to understand the biology of follicular lymphoma and develop effective treatments for the disease. A team comprised of multiple investigators from the same or different institutions working collaboratively will be required for this grant.

- **Translational Awards** — These grants aim to support clinical and/or biological research. Activities supported by these awards should lead to initiation of a clinical trial by year three of the grant.

For the RAFL-I 2024-25 cycle, a single Synergistic Team Award and up to two Translational Awards will be awarded.

These guidelines are for the STA subprogram. Please review the link below regarding the TRL subprogram to ensure you are applying to the subprogram that best suits your research. If you are unsure, please contact researchprograms@lls.org.

TRL Award: Guidelines and Instructions

Synergistic Team Awards (STAs)

A STA award intends to bring together established investigators from one or several institutions to develop a focused research program, foster new interactions and cooperation, and enhance interdisciplinary research among the participants. The overall goal of this mechanism is to enhance the development of innovative strategies for the treatment, diagnosis, or prevention of FL. Strategies that move discoveries from the bench to the clinic are of high importance as are integrated translational projects.

A major emphasis in the STA is on clinical translation of scientific results. Ideally, a STA application will propose a combination of basic and translational laboratory research that will lead to eventual clinical translation. There should be clear and direct "bench to bedside" translational trajectory from one or more of the Projects in the STA. It is important to note that the inclusion of a clinical trial in and of itself may not satisfy this requirement. Any clinical translation must be a coherent and integrated extension of other STA activities, and there should be substantive interactions and synergy between clinical trials and more basic or early translational Projects in the STA.

Each STA is comprised of 2-4 distinct but synergistic scientific Projects and 1-3 supportive Cores, including an administrative Core. There must be objective evidence of interdisciplinary research and the potential for synergy by linking the various Projects and Cores into a STA team. Prior collaboration is desirable. The quality and significance of the Projects and Cores and the enhanced productivity that is likely to be achieved by linking investigators are primary determinants of funding decisions. A STA team will be judged as a unit and funding will not be available for otherwise meritorious but non-synergistic parts of an application.

The maximum total award is $6,500,000. The maximum total annual award is $1,300,000 for each year of the five-year grant. The maximum allowable indirect cost rate is 15% ($195,000 per year). LLS and IFLI prefer a 10% indirect cost rate (or less). You may claim less than 15% indirect costs and apply the difference to the direct costs. The STA Director has the authority to budget these funds among the various Projects and Cores.

The budget must align with the actual costs of the research; this will be reviewed both by the IFLI/LLS Joint Leadership Group composed of IFLI and LLS scientific staff.

In addition to these funds, IFLI may in its discretion make up to $2.25M available in each grant cycle as awards to supplement funded RAFL Grants ("Supplemental Funds"). IFLI will not award any Supplemental Funds until at least the second year of the RAFL grants. Progress reports will serve as a means for Supplemental Funds to be requested and for such requests to be evaluated by IFLI and LLS.

Post-Award Management

Milestones and Deliverables

Annual projected milestones and deliverables are required of awarded STAs. Shortly after the funding decision is made, LLS will contact the STA Director to initiate a discussion on milestones and deliverables. These milestones and deliverables will serve as the foundation for the annual assessment and should be brief statements related to the specific aims in your

proposal. Both parties will need to agree to the final wording of the milestones and deliverables. These are due by the contract due date.

STA Team Meetings
A key element of a STA is the integration of the various Projects and Cores. STA teams should meet via teleconference or in person at least quarterly to discuss STA progress and planning.

Professional Headshot for the STA Director and Project Leaders
LLS requires submission of a photo (head shot) for the STA Director and the Project Leaders. The photos will be used alongside the Biography and Lay Description which is collected at the full application phase for publicity and fundraising purposes and displayed on the LLS and/or IFLI websites. ***The photos are due prior to the start of funding.***

Site Visits
Annual Site Visits will occur around the anniversary of the grant start date. An Evaluation Committee (LLS and IFLI scientific staff and external reviewers) will visit the STA Director and members of the STA team. The STA Director, Project Leaders and Core Leaders must be present. The STA team will present an overview of the progress made in the prior year in relation to the aims of the STA and the milestones/deliverables. Any problems encountered should be discussed and any changes from the original aims should be justified. Prior to or at the conclusion of the site visit, the STA Director must provide LLS Research staff with copies of progress presentation materials (PowerPoint decks or PDF documents) which must include descriptions of proposed goals/milestones for the upcoming grant year.

Annual Post-Site Visit Assessment
After the annual Site Visit, the Evaluation Committee will assess the progress made and the quality of synergistic activity of the STA. From this evaluation, a recommendation will be made as to the level of continued funding. In the case of well-integrated and productive teams, the funding will remain the same. In the unlikely event that progress is not sufficient, remedial actions will be discussed with the STA Director; such actions might include changes in project aims or scope and/or a reduction in future funding. After this assessment, the Evaluation Committee will work with the STA Director to establish milestones for the coming year. The outcome from the Annual Assessment will be communicated to the STA Director within 60 days of the Site Visit.

Annual STA Progress Meeting
Each year, there is a mandatory, in-person Progress Meeting for representatives from all currently funded STA and LLS SCOR Grant teams. Travel to and from this meeting should be factored into the yearly travel budget of the STA. LLS and IFLI leadership will attend.

Annual Reports
Financial, Intellectual Property, Conflict and Other Disclosures, and Progress Reports are due annually while Publication Reports are due quarterly. The Progress Report will contain a summary of the year's research and is essential for staff evaluation of progress. Release of the next STA funding payment is contingent on approval of satisfactory reports.

STA Project Replacement Policy

LLS, in consultation with IFLI, will enforce its policy regarding underperforming Projects/Cores. All Projects/Cores within a STA program are meant to contribute substantially to the overall program goals and synergize with other STA components. If a Project or Core becomes unviable or unproductive, the STA Director must notify LLS within two weeks of this determination. Alternatively, if LLS and IFLI staff judge a Project/Core to be no longer viable, they will notify the STA Director. LLS and IFLI will determine whether RAFL program goals will be best served by substituting a replacement Project/Core for the terminated one or by continuing support of the STA program with one fewer component Project/Core.

Who Can Apply?

Citizenship

The program welcomes applications worldwide from appropriate academic institutions and investigators of any nationality.

General Eligibility

Applicants must hold a PhD, MD, DVM, or equivalent degree and must be affiliated with a non-profit Institution at the time funding commences and for the duration of the award. Applications may involve multiple institutions.

Institutional Affiliation

Applicants (STA Director) must be independent investigators affiliated with a non-profit Institution. Individuals from non-academic organizations are not eligible to apply as the STA Director or Project Leads/Core Leads (but may participate as Collaborators).

Application Limitations

An applicant may submit one application per cycle as a STA Director or Principal Investigator in either or both RAFL grant mechanisms, provided that the project is unique. Applications from the same research lab that exceed the 1 + 1 limit will not be accepted. A PI or PD can serve on only one other application as a Project/Core Leader (STA) or as a Co-Principal Investigator (TRL). A Co-Principal Investigator or STA Project/Core Leader may serve as a Co-Principal Investigator or STA Project/Core Leader on a maximum of two applications. A Principal Investigator or Co-Principal Investigator can serve as a Collaborator on an unlimited number of applications.

Leadership

The STA is led by an overall Principal Investigator, called the STA Director, who is responsible for writing and submitting the application. The STA Director of a funded STA is also responsible for the disbursement of funds to the various Projects/Cores, the conduct of the Projects and Cores, and adherence with LLS policy. Each Project/Core is led by a Project Leader/Core Leader, who is responsible for the management of that Project or Core. There must be at least three but no more than four Projects. There may be one to two scientific Cores, in addition to one required administrative Core.

Leadership Limitations

STA Director

- May only submit one application as a STA Director.
- Must be a Project Leader on one proposed Project.
- Cannot be a Project Leader on more than one proposed Project.
- May be a Project Leader on one other STA application submitted per cycle.
- May or may not be a Core Leader.

Project Leader(s)

- One Project Leader must be the STA Director.
- May not be a Project Leader on more than one Project in a STA.
- May be the Project Leader on a maximum of two Projects on separate STA applications submitted per cycle.

Project Co-Leader(s)

- May be a Project Co-Leader and/or Project Leader on a maximum of two Projects on separate STA applications submitted per cycle.
- May have up to two (2) Project Co-Leaders.

Core Leader(s)

- May be a Core Leader on no more than one Core for any one STA application submitted per cycle.
- May be a Core Leader on one other STA application submitted per cycle.
- May or may not be a STA Director.

The Projects and Cores may be at the same institution or at different institutions. Either the demonstrated synergy or the potential synergy of the STA components will be a critical part of the review process.

Modifications to leadership of approved LOIs and funded STAs must be approved by LLS. Please contact researchprograms@lls.org for any change requests.

Research Environment

Investigators must demonstrate that their research environment is equipped and suitable for all aspects of the work. Applications for projects that depend on clinical samples or drugs which are not commercially available must provide documentation confirming sample or drug availability. Collaborations between multiple investigators to strengthen the work proposed will be considered favorably but are not required. Applications may involve multiple institutions; however, the Applicant will be responsible for signing off on all terms of the Funding Agreement.

Institution's Acceptance of the Terms and Conditions:

Applicants who are offered a STA award will be sent a funding agreement. This must be accepted and signed by the Applicant and by responsible institutional officials. Currently, the NIH does not accept LLS's Terms and Conditions.

Relevance:
The proposed research must be directly aimed toward advancing our understanding of and/or treatments for FL. Programs must be concerned with understanding properties and vulnerabilities of FL and/or focused on developing and testing novel FL therapies. Applications that do not meet the relevance requirement will be disqualified without full review.

Application Process & Applicant Notification

The application process will occur in two phases, the Letter of Intent (LOI) phase and Full Application phase.

Key Dates

Phase	Date
Call For Proposals	July 1, 2024
Letter of Intent Due	September 9, 2024, 3:00 PM ET
Notice of Full Application Invite	No Later than October 18, 2024
Full Application Deadline	January 13, 2025, 3:00 PM ET
Review Panel Meeting	March 2025
Notification of Awards	April 2025
Award Start Date	July 1, 2025

All submission deadlines will be enforced. Please note that all times are Eastern Time (ET). If any date falls on a weekend or US holiday, the deadline becomes the next business day.

It is highly recommended that submissions are done *prior* to the deadlines. Internet traffic may be slow near the deadlines, which may result in difficulties in submissions. In addition, LLS's response time to questions may be delayed by the high volume received near the deadlines. Therefore, it is imperative that any submissions or questions be posed to LLS as far ahead as possible.

Review Process for the Letter of Intent and Full Application

Letters of Intent for the RAFL-I STA Program are reviewed and approved by IFLI/LLS after submission. The LOI stage is a competitive step; all LOIs will be reviewed for eligibility as well as for relevance and responsiveness to the goals of the program. If invited for full application submission, the applicant will be notified by email and will immediately have access to the application submission capability in the LLS Research Portal. If you have not received an email regarding your LOI by **October 18th, 2024**, contact researchprograms@lls.org.

Full applications received by the January 13, 2025, 3 PM ET submission deadline will be reviewed by the IFLI/LLS Joint Leadership Group for responsiveness to the RAFL program goals and adherence to the application guidelines. An application that does not meet the program goals, scope, or guidelines will be administratively disqualified.

Full applications will be reviewed by a peer review committee composed of a diverse group of external experts. Applications will be evaluated according to the Review Criteria listed below and assigned an initial score by the primary and secondary reviewers. Only applications that fall above a scoring level determined by program staff and the committee chair will be discussed in detail for final ranking by the entire committee. Once ranked by the peer review panel, the highest scoring proposals will be reviewed by LLS and IFLI research staff. LLS and IFLI will identify those proposals to be funded based on scientific merit, responsiveness to programmatic goals, and budget availability. Final approval of funding will be made by the Oversight Boards of the IFLI and LLS.

Review Criteria for Full Application

An application receives a Priority Score based on a 9-point rating scale (1=most meritorious; 9=least meritorious) using the criteria outlined below. This score reflects the STA proposal as a unit and is not based on any individual project in isolation.

- The significance of the proposed research to the diagnosis, treatment, or prevention of Follicular Lymphoma and/or relevant premalignant conditions.
- The qualifications of the STA Director and Project/Core Leaders.
- The synergy that will likely result from the interactions of the Projects and Cores; **it is critical that the STA be more than a collection of high-quality Projects/Cores- that must be weaved together with a common theme with clear interactions between them that should result in synergy.**
- The quality of the Cores and their ability to support multiple projects; the Cores should not be research oriented as the Projects are. Appropriate Cores may be animal modeling, sequencing/informatics, clinical trial support, etc.
- The quality and relevance of the preliminary data.
- The perceived feasibility of the proposed experimental and investigative approaches.
- The likelihood that the research findings will lead to eventual clinical application, ideally within the period of STA funding or soon after the funding period.
- The quality of the resources and environment.

- The alignment of the quality of and access to patient populations and/or patient specimens with the research plan (where applicable).
- The clarity of thought and presentation, including an adequate number of figures that clearly present the data. **Each Project must have a minimum of three figures.**

Any Applicant selected for funding will be notified by the date indicated in the Key Dates section. Please do not call or email IFLI or LLS to determine whether the application has been received, when it will be reviewed, or the results of the review. Please check the LLS Research Portal for the status of your application. Final scores are confidential and are available only to IFLI Board of Directors and administrative staff, LLS staff, LLS's Medical & Scientific Affairs Committee and its Research Subcommittee, and LLS's National Board of Directors.

If there is a person that you would like excluded from reviewing your LOI and/or full application, please email researchprograms@lls.org no later than the LOI deadline of **September 9, 2023**. LLS will make every effort to accommodate these requests but cannot guarantee such exclusion(s).

General Application Instructions

All submissions must use the LLS Research Portal at https://lls.fluxx.io. It is recommended that you familiarize yourself with this portal well in advance of any deadlines.

Registration
Both the applicant and institution must be registered in the LLS Research Portal. If you have applied to LLS in the past, you do not need to create a new registration. Simply log in with your username and password. If you forgot your password, click the "reset or create password" link and enter your email address. The system will send your username and a link to update your password. Once updated, the applicant can begin the LOI. If you are a first-time user to the LLS Research Portal, please complete the intake form located at this link: Account Creation Request so an account can be created for you. Only LLS staff members have administrative permission to create new accounts.

Institutional Designation
Applicants should create their profile from the standpoint of where they will perform their research described in the application. The applicant must indicate the name of the institution as well as the name of the signing officials for that institution. If your institution is not displayed as an option under this field of the application, you may contact researchprograms@lls.org to have it registered in the system. Please provide the official's full name and email address.

Data Entry
Both the LOI and the full application may be accessed and changed multiple times as needed prior to the submission deadline. However, neither the LOI nor the full application can be changed once the respective deadlines have passed or the final application has been submitted. Moreover, some fields may not be modified in the full application following submission of the LOI.

Forms and Format
Applicants will provide information on the LLS Research Portal and downloadable templates at the LOI and full application phases. All information must be typed in English using commonly accepted grammar and punctuation. Some information will be captured when applicants populate fields on the LLS Research Portal. Fields in bold are required.

Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template.

Font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself. *If character limits, font restrictions, margins and/or page limitations are not adhered to, the application may be administratively disqualified.*

In case there is a discrepancy between the application template and the guidelines document, the downloadable template supersedes the guidelines.

Contacting LLS
Questions that are not clarified in this document or the LLS Research Portal should be addressed to researchprograms@lls.org.

Beginning an application
The application will be completed in two phases: Letter of Intent and Full Application. Below are step-by-step instructions for applying:

1. Read these Guidelines & Instructions in full and familiarize yourself with the LLS Research Portal.

2. Log into the LLS Research Portal, and under “Information” in the left navigation bar, select Research Accelerator for Follicular Lymphoma program. Click "Apply to RAFL!" to begin the application process (well ahead of the deadline).

3. Click “Edit” and follow the instructions for each web form field. Bold font indicates required information.
    - Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. If character limits are not adhered to, the application may be disqualified.
    - You may save your work and return to it at any time by clicking “Save.” Clicking “Submit” will lock your application and prevent further modification at that stage. Contact researchprograms@lls.org if you submit in error (must be before the deadline).

4. Once your LOI is submitted, you will receive an automated confirmation email within two business days from the LLS Research Portal. Consider that these emails may end up in your spam filter.

5. If your LOI is selected, you will have access to the full application. Click on your request, found in *New* or *Pending*, to continue with your application.

6. Please carefully follow the instructions on the LLS Research Portal and this document. Full applications require completion of both the web form and the application template, which should be downloaded from the *Project and Supporting Documentation* section of the LLS Research Portal. **Failure to follow all application instructions may result in administrative disqualification of your application.**

7. Submit your full application to the LLS Research Portal prior to the full application deadline. **We strongly recommend submitting well before the deadline, as site traffic on the day of and days leading up to the deadline will be heavy.**
    - Contact researchprograms@lls.org with any questions about the application phases that are not addressed in the LLS Research Portal, the FAQ, or this document.

8. To create a fair process to all applicants, these Guidelines & Instructions and information on the LLS Research Portal must be followed. ***Do not ask for exceptions to these policies, including but not limited to exceptions to deadlines or making corrections to your document past the deadline.***

Carefully check every page of your application prior to submission. You are ultimately responsible for this submission, even if someone else submits your final application.

At any time during the application process, including after submitting your full application, you can check the status of your application by logging into the LLS Research Portal, selecting your application (under *Requests* in either "New or Pending" or "Submitted") and referring to the status in the yellow box at the top of the page.

If you have any technical difficulties with the LLS Research Portal, please contact researchprograms@lls.org.

Detailed Letter of Intent Phase Instructions

The LOI must be submitted by **September 9, 2024, at 3:00pm ET** via the LLS Research Portal or the following business day if this date falls on a weekend or a U.S. holiday. The Applicant should carefully craft the information requested in the LOI as this information is automatically populated into the full application and is subject to the Changes clause listed below.

The LOI will be evaluated by the IFLI/LLS Joint Leadership Group. If the LOI is approved, the Applicant will be notified by an automated email from the LLS Research Portal stating that they may proceed to the Full Application phase. Applicants may also check the status of their LOI on the LLS Research Portal.

There are two main aspects to the Letter of Intent Phase: all LLS Research Portal webform fields and the "Previous Studies/Preliminary Data" (2 pages maximum) downloadable template for completion.

The LOI presents a description of the overall scientific problem and the integration of the various

Projects and supporting Cores.

The LOI is reviewed for responsiveness to the goals of the STA, and include:

- **qualifications of the STA Director and Project Leaders**
- **significance of the research to follicular lymphoma**
- **quality of each Project and Core including preliminary data**
- **the likelihood of synergy among the Projects**
- **the significance of each Core to multiple Projects**
- **the likelihood of near-term clinical translation**

Organization Information

(If the institution or officials are not listed, please contact researchprograms@lls.org with the name and email address for the official you need added)

Institution: Indicate the name of the institution where the research will be performed. If this institution is not listed, please contact researchprograms@lls.org with the institution name and address so an account can be created.

Location/Department: This field auto populates. Please do not change it.

STA Director: The STA Director is the applicant.

Institutional Signing Official (ISO): The ISO is the institutional representative responsible for signing and agreeing to the accuracy of the application and the terms and conditions of the award, should the application be selected for funding.

Financial Officer: The Financial Officer is the institutional representative responsible for the financial administration of externally funded research.

Additional Access (Admin/Assistant): Access may be given to personnel to assist in the application process. This is the institutional representative responsible for the day-to-day administration of externally funded research (or the Research Administrator).

Technology/Transfer Official (TTO): The TTO is the institutional representative responsible for overseeing Intellectual Property.

Additional Contact (Assistant): This is optional and may be a personal representative of the principal investigator, such as an administrator, an assistant, or a laboratory manager to be used as an additional point of contact, typically in the post-award phase. The Additional Contact will not have access to the application in Fluxx.

Zip Code of the Institution: Enter the zip code of the institution if located within the United States. You will need to select the zip code from the drop-down menu to ensure it is captured in the zip code field. Leave this blank if the institution is not located within the US.

Program Information

STA Director Name and Scientific Degree

STA Director Job Title

STA Title – Provide a title adhering to the 150-character limitation (which includes spaces).

STA Scientific Abstract – The applicant should provide an overview of the proposed STA program. Describe the overall proposed research and a brief overview of each Project and Core. Discuss the interaction between components that will create synergy. Discuss plans for clinical translation of findings. Describe the potential impact of your study on follicular lymphoma, and the patient's experience. Describe the timeframe in which the benefits may be realized. Scientific/Greek symbols or characters must not be used. (Maximum 6,000 characters including spaces.)

Amount Requested – Enter the total amount of funding requested over the life of the grant (maximum of $6,500,000). The amount requested on the LLS Research Portal should match the budget sections of the full application template. The total amount, including both direct and indirect costs, cannot exceed $1,300,000 per year. Please note that LLS does not follow the NIH guidelines for budgets.

Individual Information for STA Projects 1-4

- **Project Title** – Provide a title adhering to the 150-character limitation (which includes spaces).
- **Project Scientific Abstract** – Using technical language, briefly describe the proposed research (maximum 3,000-character limit including spaces for each Project). Scientific or Greek symbols may not be used. Once the LOI has been submitted, the Scientific Abstract cannot be changed.
- **STA Project Leaders** – The STA Sub-Program must be comprised of at least 3 but not more than 4 Projects. The following information must be provided for each Project Leader:
    - Name – The Project must have a single, designated Project Leader.
    - Degree
    - Institution
    - Job Title
- **Project Co-Leaders** – Project Co-Leaders are optional. Projects may have up to 2 Co-Leaders. Supply the following information for each Project Co-Leader:
    - Name
    - Degree
    - Institution

Individual Information for the STA Program Cores

The Program must have one Administrative Core. You will also have the option of having up to two (2) Scientific Cores. Cores serve supportive functions and cannot be research oriented.

Administrative Core Information

- **Description** – Provide a brief description of the Core's activities (i.e.; Goals, Function/Operation, Benefit and relation to other STA components)
- **Administrative Core Leader**
    - Name
    - Degree

- Institution

Information for Scientific Core Projects A-B

- **Designation** (i.e., animal facility…) – 150-character limit including spaces.
- **Description** – Provide a brief description of the Core's activities (i.e., Goals, Function/Operation, Benefit, and relation to other STA components)
- **Scientific Core Leader** – Provide this information for each Scientific Core.
  - Scientific Core Leader Name
  - Degree
  - Institution
- **Core Co-Leaders** – Projects may have up to 2 Core Co-Leaders, they are optional. Supply the following for each Core Co-Leader.
  - Core Co-Leader Name
  - Degree
  - Institution

STA Program Collaborators/Key Personnel

Indicate any personnel, outside of your institution, with whom you have significant and current interaction regarding your project. Only include those people who are at or above tenure-track level (or equivalent). List up to (5) five people including name and institution.

Proposed Start Date: The start date for STAs is July 1, 2025.

Proposed End Date: The end date for STAs is June 30, 2030.

Previous Submission: Indicate whether you have previously submitted a similar proposal to LLS and indicate the date of any prior submission.

Previous Studies/Preliminary Data: Upload the Previous Studies/Preliminary Data (2 pages maximum) to the "Project and Supporting Documentation" section of the web form. Text, figures, and references must be written single spaced in Arial size 11 font. Text within figures should be easily readable without magnification. Please note that references are not required at the LOI phase but are required at the full application phase. Only one PDF is accepted in this section, so delete any other documents uploaded during the process. **Note**: When uploading this template to the LLS Research Portal, please ensure you choose the correct file name which should read "Previous Studies/Preliminary Data" which you can choose from the document upload drop-down menu. If the file name is incorrect, you will not be able to submit the LOI. In addition, when you name your file, please only use underscores or spaces to separate words.

All LOI required forms must be consolidated into a single PDF file and uploaded to the Project and Supporting Documentation section of the LLS Research Portal.

LOI Save, Review, and Submit Instructions

Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

After clicking "Save" you will be directed to review your LOI. Please ensure all information is accurate, and then click the "Submit" button to submit your LOI to LLS.

Each applicant must submit the LOI by **September 9, 2024, at 3:00 pm ET** via the LLS Research Portal. After clicking the "Submit" button, the applicant will receive an automated email within 2 business days stating that your information was successfully submitted. If you do not receive the email from the LLS Research Portal within two business days of LOI submission, please e-mail researchprogram@lls.org. Signatures of the applicant and institution officials are not required for submission of the LOI.

The applicant is ultimately responsible for the submission, regardless of who actually is uploading information on the LLS Research Portal. Every year, LLS has a small number of people that notice problems with their letter of intent after the deadline. The solution to this problem is very simple and in the hands of the applicant:

- **Check your letter of intent prior to final submission.**
- **Submit well ahead of the deadline.**
- **We are not responsible if any applicants are unable to submit by the deadline if our system indicates that:**
  a. **the letter of intent procedure was started less than 24 hours before the deadline,** or
  b. **a previously started letter of intent file was then only picked up again less than 3 hours before the deadline.**

Changes
Information collected in the Letter of Intent Phase will automatically populate fields in the full application. Once submitted, changes may only be made after receiving prior approval from LLS. The applicant must email researchprograms@lls.org requesting any change and identifying the elements to be changed. Any changes made without the prior approval of LLS may result in the disqualification of the application.

Detailed Full Application Phase Instructions

Each invited applicant must submit a full application by **January 13, 2025 at 3:00 pm ET** via the **LLS Research Portal** at https://lls.fluxx.io or the following business day if this date falls on a weekend or U.S. holiday. Most sections of the full application will carry through from the LOI Phase. Information that carries through must not be modified; changes cannot be made to the LOI components after the LOI Phase deadline. The remainder of the full application consists of web form components and elements to be uploaded as a ***single PDF***.

The Full Application is a more complete description of the STA. There should be no changes to the original intent, aims, or leadership between the LOI and the full application.

Failure to submit as a single PDF in the order below may result in disqualification of the application.

Two sections are required in the uploaded PDF:

Section 1: Project Description
Download and complete the project description template, including all required signatures, and upload to the "Project and Supporting Documentation" section of the web form. Margins are preset and must not be changed. Text, figures, and references must be written single spaced in Arial size 11 font. Embedded figures must be legible.

Only one application PDF is accepted at the full application phase (Project Description Template combined with biosketch(es) and all applicable appendix documents). Do not delete the LOI "Previous Studies/Preliminary Data/Trial Summary" PDF file.

The template consists of the following required elements:

1. **Program Information Cover Page (see template for detailed instructions)**

2. **Public STA Program Information**: If awarded, your information will be featured on LLS.org for the duration of the award. Please do not use any graphical elements, such as figures or charts. The use of Greek characters or symbols is also not permitted in this section. The Public Grant Information is essential for LLS to continue successful fundraising to support our current and future grantees, including the later years of your award, should it be funded. Thus, we require a well-written lay section, with sufficient detail and suitable language for non-scientists. This section should clearly state the relevance of your research to follicular lymphoma and describe your current/proposed research, including the problem/question to be addressed, specific aims, and anticipated results using non-technical language that is easily understood by the lay community. Be aware of your confidential information, as the Lay Description, and Project Summary and short bios will be shared with others.

   a. **Overall STA Program Summary:** Provide a short summary in lay language (approximately 1,500 characters including spaces).

   b. **Overall STA Program Lay Description**: Longer lay summary (maximum of 3,000 characters, including spaces).

   c. **Brief Biography of the STA Director:** Provide a brief, professional biography introducing the STA Director to a lay audience (maximum 1,000 characters including spaces).

   d. **Individual Project Summaries:** Provide a short summary (2-5 sentences) in lay language for each STA project.

   e. **Individual Project Lay Description:** Longer lay summary for each STA project (maximum of 3,000 characters including spaces for each project).

   f. **Brief individual biographies of the Project Leaders:** Brief professional biography introducing the Project Leaders to a lay audience (maximum of 1,000 characters with spaces for each Project Leader).

3. **Graphical Abstract**: Provide one or two graphical abstract(s) to succinctly describe the organization and key focus/themes of your proposed STA program. This graphical abstract provides reviewers with a quick overview of your research plan. This is similar to the graphical abstract in a Cancer Cell paper. Limited to one (1) page.

4. **STA Justification and Major Resources** (see template for detailed instructions)

5. **Projects** (see template for detailed instructions)

6. **Cores** (see template for detailed instructions)

7. **Budgets for Projects and Cores**
   The Budget and Budget Justification should provide itemized detail for each major category for all years of the Projects/Cores. The budget can be summarized in year one and extrapolated for the remaining years. All totals and subtotals should be completed on the form.

The aggregate costs over five (5) years cannot exceed $6,500,000. The maximum annual total cost (direct and indirect) cannot exceed $1,300,000.

Permissible Direct Costs include the following with the specified limitations:

- Personnel Expenses including salary, wage, or stipend with fringe benefits.
- Supplies & Materials requests should be itemized by category.
- Equipment Purchase requests must identify each item of equipment with an acquisition cost of more than $4,000.
- Travel Expense requests cannot exceed $10,000 per year of the award.
- Other Direct Cost requests can include patient care costs.

Permissible Indirect Costs (often referred to as Institutional Overhead, IDC, M&A, G&A, or pooled costs) are those costs incurred for common or joint objectives that cannot be readily identified with a particular project (general maintenance, utilities, library, etc.) as defined in the Office of Management and Budget, Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards. ***Indirect costs rates of 10% or less of total annual costs are preferred; if not feasible, the maximum indirect cost rate is 15% of annual total costs.*** For institutions that do not choose to use these funds for indirect costs, LLS allows the funds to be applied to the program's direct costs.

8. **Subaward budgets** should be included within the main budget line items. Indirect costs can be included in the total indirect costs. Please note, LLS will only pay the funded institution, and that funded institution will be responsible for all subcontracting and subsequent payments.

9. **Impermissible Costs** include membership dues, tuition, books, journals, and publication costs.

10. **Budget Justification** Two (2) page maximum for Projects and two (2) page maximum for Cores.

11. **Signature Page** This form must be completed, including the indicated signatures.

Section 2: Appendix

The following sections must be attached in this order to the end of the project description template to create a single PDF. ***No other information may be provided in this section.***

a. **Biosketches and Other Support (Required for the STA Director, Project and Core Leaders only).** Use the most recent NIH Biosketch format and include the NIH Other Support form found on the NIH website. An eRA Commons username is not required. The Other Support section must contain all current and pending support from any source. The section of the Biosketch containing the Research Support section may be used, but all current and pending support must be included; completed support should not be included. As per the NIH format, the goals of each grant must be stated. **In addition, specific aims must be listed for current and pending grants that may overlap or appear to overlap with your STA Application**. This includes any grants or portions of grants submitted to any organization, including LLS.

   If funding decisions about potentially overlapping, pending grants become available following submission of an LLS application, LLS must be notified within five business days of the applicant's receipt of that information; please e-mail researchprograms@lls.org.

   IFLI and LLS recognize that some investigations, particularly those involving clinical trials, may require multiple funding sources, so overlap of specific aims with another grant may be appropriate and acceptable. The need for and details about such overlap should be clearly explained in the application. However, IFLI/LLS will consider an applicant's other current grant support in its funding decisions. This may result in IFLI/LLS funding only part of the grant or none of the grant, depending on the level of overlap. In addition, IFLI/LLS reserves the right to adjust the level of funding of an awarded grant should another overlapping or potentially overlapping grant that was pending at the time of grant submission be awarded to the applicant.

   Failure to abide by LLS's rules on disclosure of current or pending support may jeopardize the funding of the current application and may affect future LLS funding decisions.

b. **Collaboration/Support Letters**
   Required if reagents critical for the research are to be obtained from non-commercial and/or commercial sources and are not currently available in your lab.

c. **Clinical Trial Summary (Required where applicable) and optional Clinical Protocol Synopsis (not to exceed 8 pages)**
   Provide a **one-page summary** and a link to the clinicaltrials.gov website for any clinical protocol essential to the proposed research. Include IRB approval date, IRB compliance number, and effective dates of approval. Projects for which IRB approval is pending must include a statement to that effect. The applicant should notify researchprograms@lls.org of IRB approval prior to the grant review. Optional: include a Clinical Protocol Synopsis. DO NOT include the full clinical trial protocol.

   The applicant must provide information **if a trial is receiving funding from a sponsor,**

specifically, how much money is to be received and what the funds will be used for.

Full approval for any IRBs that are necessary for the research must be obtained by the award start date.

d. **Assurances (Required)**

Human Subjects:
The applicant must indicate if human materials or subjects will be involved in the proposed research. The status (approved, pending, or exempt) of the Institutional Review Board (IRB or equivalent oversight entity) approval must be provided. The Human Subject Assurance Number (OHRP) must be included. If the research project has received IRB approval, the date must be provided, and documentation must be included in the single PDF of the application.

If a project is exempt from IRB review, the certificate of exemption must be included in the single PDF of the application.

Laboratory Animals:
The applicant must indicate if laboratory animals will be involved in the proposed research. The status and date of Institutional Animal Care and Use Committee (IACUC or equivalent oversight entity) approval must be provided. The Animal Welfare Assurance number must be included. Documentation of institutional approval must be included in the single PDF of the application. The application may be submitted with IACUC approval pending but an award will not be made without documented IACUC approval if it was pending at the time of application submission. It is recommended that the applicant notify LLS before the grant review if the IACUC status has changed.

Recombinant DNA:
The applicant must indicate if the proposed research involves the use of recombinant DNA. Documentation of institutional approval must be included in the single PDF of the application.

Biohazard Statement:
The applicant must indicate if the proposed research involves the use of biohazards. If the applicant indicates affirmatively, then an institutional statement of assurances regarding potential biohazards and safeguards must be included in the single PDF of the application.

Your institution is required to have assurance procedures in place, so please check with them if you are unsure how to obtain your assurance approval documentation.

No attachments besides those listed above can be included in the Appendix. Applications that include additional documents besides those requested may be administratively disqualified.

Uploading the project document and final submission
All documents must be combined into a single PDF in the order listed above. Failure to submit as

a single PDF in the order above may result in disqualification of the application. Upload the full application components, as a single PDF, in the "Project and Supporting Documentation" section on the web form. The file upload should be labeled, "STA Project Description/Application" which you can choose from the document upload drop-down menu.
Do not delete the LOI "Previous Studies/Preliminary Data/Trial Summary" PDF file.

LLS Research Portal Webform Updates

- **Project and Core Details**
  Provide the required information within the LLS Research Portal webform.

- **Budgeting Information**
  Enter the budgeting information as required on the web form fields.

- **Assurances**
  Respond to the assurance questions and indicate if approvals are pending or the date of approval with the approval number.

- **Applicant Assurance**
  Check the box to accept the terms as stated on the web form field.

Save and Review
Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

Submission & Confirmation
After clicking "Save" you will be directed to review your application. Please ensure all information is accurate, and then click the "Submit" button to submit your application to LLS. Only one application document and one Letter of Intent request document should be present. If extra documents remain after submission and before the deadline, email researchprograms@lls.org and let us know which documents to remove. You will receive an automated email **within 2 business days** stating that your information was successfully submitted. **If you do not receive the email confirmation of submission, contact LLS at** researchprograms@lls.org.

Carefully check your PDF prior to submission. If you notice problems with your PDF after you have submitted, email researchprograms@lls.org, and we will help you upload the correct document or delete any incorrect documents. This email must be received, with the correct document, prior to the deadline; there are no exceptions to this rule.

The applicant is ultimately responsible for the submission, regardless of who actually is **uploading information on the LLS Research Portal.** Every year, LLS has a small number of people that notice problems with their application after the deadline. The solution to this problem is very simple and in the hands of the applicant:

- **Check your application prior to final submission.**
- **Submit well ahead of the deadline.**
- **We are not responsible if any applicants are unable to submit by the deadline if our system indicates that:**

a. **the application procedure was started less than 24 hours before the deadline,** or
b. **a previously started application file was then only picked up again less than 3 hours before the deadline.**

Once the deadline has passed, only the following updates may be made:

- Regulatory approvals
- Significant updates to clinical trials:
  - IRB updates
  - Opening of the trial
  - Patient enrollment
  - Opening of new clinical sites
  - Efficacy and/or safety updates
- Manuscripts that are accepted for publication; the following must be provided via email to researchprograms@lls.org:
  - Complete list of authors as they appear on the accepted manuscript with your name in bold
  - Manuscript title
  - Journal
  - Date of publication or online ahead of print (if known)
  - A copy of the acceptance letter from the journal
- Updates regarding any transfers to a new institution

If you plan to withdraw your application at any time during the application cycle, please inform staff of your decision by writing to researchprograms@lls.org.