Cystic Fibrosis Lung Transplant Consortium
2016 LOI and Full Application

POLICIES AND GUIDELINES

July 27, 2016
I. MISSION
The mission of the Cystic Fibrosis Foundation (CFF) is to cure cystic fibrosis and to provide all people with the disease the opportunity to lead full, productive lives by funding research and drug development, promoting individualized treatment, and ensuring access to high-quality, specialized care. To meet this mission, various types of grants are offered to support meritorious research ranging from basic laboratory investigation to clinical management of CF.

II. BACKGROUND
Although median predicted survival in CF has steadily increased over the last several decades, lung transplantation remains an important consideration for many individuals with CF and end stage lung disease. With median survival after lung transplant only modestly improving over the last decade, and chronic lung allograft dysfunction being a consistent challenge and major cause of mortality for lung transplant recipients, new approaches to improve long term outcomes after lung transplantation are needed. In addition, variations in the selection and care of lung transplant candidates suggests opportunities exist to identify best practices that in the short term may improve access to transplant and patient outcomes.

III. CF LUNG TRANSPLANT CONSORTIUM AWARD OVERVIEW
Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT), a non-profit affiliate of Cystic Fibrosis Foundation, will provide up to $125,000 per year, plus indirect costs of 8%, for up to three years to establish a clinical and translational network of CF lung transplant centers (CFLTCs).

Application for support of these projects requires a two-step process. An applicant must first submit a letter of intent (LOI) by the announced deadline. Upon notification of acceptance, selected applicants will be invited to submit a full application.

IV. OBJECTIVES AND SCOPE
The objective of this proposal is the establishment of a clinical and translational research network of CF lung transplant centers (CFLTCs) to facilitate the study of lung transplant for CF and other lung diseases to improve access, clinical care, and long term outcomes of individuals with CF who undergo lung transplant. The initial award is designed to provide support for research personnel which will allow sites to successfully contribute to projects with the following goals:

1. Initiate an observational study of lung transplant candidates and recipients to identify and develop best practices for the care of CF lung transplant recipients. Sites will be expected to share their clinical protocols to identify the variations in practice and thereby inform discussions on standardizing post-transplant care, with the goal of improving quality of care and providing a baseline on which interventions can optimally be tested. Critical to the observational study will be the sites’ contribution to a longitudinal database of detailed pre- and post-transplant clinical information that will enable observational studies of post-transplant complications and risk factors for complications. Clinical data will include demographics and insurance information; medication use; pulmonary diagnostic tests, including pulmonary function, imaging and bronchoscopy results; complications and treatments. Data from lung transplants for all patients with CF, and a selected population of patients who receive transplant for other indications, will be included.

2. Create a biorepository of prospectively collected, serial samples of blood, urine, bronchial washes and bronchoalveolar lavage, and when feasible, bronchial brushes and transbronchial biopsies. Samples in the biorepository will be linked to the database to facilitate discovery of biomarkers for transplant complications with a focus on chronic lung allograft dysfunction (CLAD).
3. Each CFLTC will be expected to conduct clinical trials within the network including:
   a. Enrollment of eligible subjects, accurate collection, storage, and shipping of biospecimens, completion of study procedures, appropriate reporting of adverse events, and compliance with regulatory guidelines.
   b. Entry, verification, and transmission of clinical study data to the CFLTC data base
   c. Additional activities may include serving as lead site for studies that use the clinical database and biorepository, performance of specialized procedures for biomarker and outcome measure development and contribution to the development of clinical protocols for conduct by the network.

4. It is envisioned that the consortium will include approximately 6-8 CFLTCs with a subset of sites with specialized expertise in translational clinical research. Further expansion by adding other care centers may be considered in the future.

5. This program will provide infrastructure support to ensure staffs’ ability to collect and contribute data and specimens to the projects outlined above.

6. When needed, separate awards to support conduct of additional trials or specialized procedures will be offered.

Paramount to success of the network and a requisite for funding include the following shared principles:

- Protecting the safety and rights of individuals and patients involved in clinical research is essential.
- The network sites commit to maximize the efficient use of resources for study development and conduct and to optimize patient access to clinical trials of therapeutic approaches.

V. ELIGIBILITY

United States residents and Canadian residents are welcome to apply.

CF Lung Transplant Center (CFLTC) Qualifications
1. Transplant Center qualifications and experience
2. Research facilities and transplant research experience
3. Research staff focused on lung transplant research
4. Experience in CF
5. Ability to perform specialized procedures and collect biospecimens
6. Institutional environment supportive of transplant research

VI. STUDY PERFORMANCE METRICS AND QUALITY IMPROVEMENT

Once a site is operational, the Coordinating Center will assist the CFLTC Steering Committee in the development and management of an ongoing site evaluation process. Minimum guidelines and criteria for assessment of performance for study conduct will be established by the CFLTC Steering Committee. The criteria established will be primarily objective in nature (e.g., enrollment, timeliness of IRB approval and contract execution, timeliness and completeness of clinical data entry). Sites will be requested to enter enrollment and start-up metrics information into a database on a quarterly basis to ensure that
the Coordinating Center and CFFT have a clear picture of current activities at a site. Additional criteria will allow some input by the Coordinating Center and biorepository director to evaluate such key factors as site responsiveness, protocol violations, and data and sample quality.

Reports will be provided to each site that will allow each site to see how their enrollment numbers compare to other sites. These reports should be used to institute Quality Improvement initiatives, when applicable.

VII. FUNDING
This award is envisioned as a three-year award, with an annual renewal based on acceptable performance. Sites approved for CFFT funding as a CFLTC will receive infrastructure support to ensure staff continuity and efficiency in the conduct of the described projects and clinical trials. The infrastructure support during Year 1 of the award will be up to $125,000. Applicants may request indirect costs of up to 8% on allowable costs.

The size of the center and required number of personnel may impact the total funding amount. This amount can support a Research Coordinator (RC) position devoted to lung transplantation (or a portion of two RCs devoted to lung transplantation to ensure appropriate coverage), and up to 10% effort of the Principal and other key Investigator’s (PI) effort to protect time for consortium work. The distribution of these funds is at the discretion of the PI and could include secretarial/administrative support, technician support, or specialized training if they are shown to advance consortium activities. If the funding is used to support other staff, there must be assurances of the commitment, continuity and availability of the PI and RC to participate in the observational study and all other networks affairs, including conduct of clinical studies and trials that emerge from the Consortium.

While additional funding will be granted for specific larger research projects, this funding is designed to assure the availability of CFLTC site research staff to participate in core CFLTC projects. Year 2 and 3 funding will be dependent upon satisfactory progress. In addition, CFFT may elect to base a percentage of the second year of funding and all subsequent funding years on performance during the preceding year.

Additional funding to the site may be available from the following sources:

- Selected site will be provided supplementary funding for the support of specialized services provided to the CFLTC (e.g., cell and RNA isolation and other methods for immunophenotyping).
- Compensation will be provided for selected committee responsibilities.
- Conduct of interventional clinical trials.

VIII. RELATIONSHIP WITH CF FOUNDATION AND CFFT THERAPEUTICS
The network is expected to have a close working relationship with CFF and CFFT. The Senior Vice Presidents of Therapeutics Development and Clinical Affairs will serve as members of the Steering Committee. Funding of the network, the coordinating center, and each of the centers will be reviewed annually, and continuation of funding is contingent upon satisfactory performance and availability of funds.
IX. SUBMISSION INFORMATION & GENERAL TIMELINE
Application for support of these projects requires a two-step process. An applicant must first submit a letter of intent (LOI) online by Monday, September 5, 2016. If the LOI is accepted, applicants will be invited to proceed to the full online application.

General Timeline:

RFA Release ................................................................. July 22, 2016
Letter of Intent Due ......................................................... September 5, 2016
Notification/Invitation to Submit Full Application ................................ September 30, 2016
Full Application Deadline ............................................... November 9, 2016
Review Committee Meeting ................................................... mid-December 2016
Applicant Notified/Award Letter Issued .................................... late December 2016
Earliest Start Date for Awarded Projects .................................... January 1, 2017

X. REVIEW AND AWARD
Applications will be reviewed by a CFFT ad hoc review committee. Formal award of programs is based upon the availability of funds, the merit of the application, and the recommendations of the reviewers. All awards will be made in compliance with the regulations and CFFT policies related to the program.

Sites will initially submit a Letter of Intent. Sites with approved LOIs will be invited to submit a more detailed application addressing the items listed below.

1. Review Criteria. Applications will be evaluated on:
   a. Transplant Center qualifications, experience, volume and waitlist details
   b. Available research facilities, and previous transplant research experience
   c. Narrative describing vision for site’s contribution to CFLTC
   d. Ability of Research Staff to focus on lung transplant research within the CFLTC
   e. Experience and volume of lung transplants performed in the last five (5) years for CF
   f. Expertise in Lung Transplant Related Specialized research procedures
   g. Institutional environment supportive of transplant research

2. Additional Expectations
   a. Ability to network with other lung transplant centers
   b. Institutional commitment to facilitate the contract process
   c. Provide regular updates on study team changes, site capabilities and study participation
   d. Responsive to requests for information from the CFFT or Coordinating Center
   e. Participation on committees
   f. Attendance at Transplant Consortium meetings

XI. LETTER OF INTENT SUBMISSION GUIDELINES – DEADLINE Monday, September 5, 2016, 11:59 PM (Eastern)

- Font: Times New Roman 12 or Arial 11 font
- Margins: Standard ½”
- When all the documents have been uploaded to proposalCENTRAL, the system will compile them into a single PDF file in the correct sequence
Letters of Intent must be submitted online at proposalCENTRAL: https://proposalcentral.altum.com.
Late submissions will not be accepted.

The Foundation reviews all LOIs electronically, and only the documents submitted online will be reviewed. All required application templates are available for download at proposalCENTRAL.

Cover Letter (template available for download): A PDF copy of the signed, cover letter should be emailed to awards@cfft.org on the date of submission.

Budget Summary (complete online): The budget may not exceed $125,000 in direct costs per year (plus 8% indirect costs) for a maximum of three (3) years.

Project Opportunity Summary (template available for download): A brief summary of your potential to participate as a CFLTC should be completed using the “Opportunity Summary Form Template” available for download on proposalCENTRAL. (Not to exceed three (3) pages).

Each site should complete a two to three-page summary with one short paragraph addressing each of the following seven topics:

1. Transplant Center qualifications, experience, volume and waitlist details
2. Available research facilities, and previous lung transplant research experience
3. Narrative describing vision for site’s contribution to CFLTC Consortium
4. Ability of Research Staff to focus on lung transplant research within the CFLTC
5. Experience and volume of lung transplants performed in the last five years for CF
6. Expertise in lung transplant related specialized research procedures
7. How Institutional environment is supportive of transplant research

Biosketches of Key Personnel (template available for download): A biographical sketch must be completed for all key project personnel. CFFT defines “key personnel” as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project. Biosketches should not exceed five (5) pages.

If the Lung Transplant Director is not the PI of the application, a letter of support for the application by the Director must be provided. (upload if applicable)

An ad hoc CFFT Committee will review letters of intent and notify applicants as to the suitability of the proposal. Please contact the Grants and Contracts Office at awards@cfft.org or 301-841-2614 if you have any questions regarding the program.

Upload Confirmation: You will receive an e-mail confirmation from proposalCENTRAL (not from CFFT) that your Letter of Intent has been successfully submitted. This e-mail will be your only acknowledgement. If you do not receive this acknowledgement, please contact proposalCENTRAL immediately to ensure that your submission is processed.

XII. FULL APPLICATION GUIDELINES - DEADLINE Wednesday, November 9, 2016, 5:00 PM (Eastern)

Sites with approved LOIs will be invited to submit a more detailed full application online.

• Font: Times New Roman 12 or Arial 11 font
• Margins: Standard ½”
• When all the documents have been uploaded to Proposal Central, the system will compile them into a single PDF file in the correct sequence
Log-in at proposalCENTRAL: https://proposalcentral.altum.com/. If you cannot remember your password, click on the “Forgot Password” button. Note: There is a Customer Service link on the top right of each screen to use as needed.

The full application will only be available to individuals who have been notified that their LOI was approved. Upon logging in please select the Manage Proposals tab to the right of screen, and then select the In Progress tab towards the left. Within this view you will see your started application per your approved LOI. Click Edit to begin the full application.

Applications must be submitted through proposalCENTRAL, https://proposalcentral.altum.com/ by 5:00 pm (Eastern) on Wednesday, November 9, 2016. Email a pdf copy of the signed Face Page (see below) to awards@cfft.org by the same date. Late applications will not be accepted and the deadline will not be waived. The Foundation reviews applications electronically, and only the documents submitted online will be reviewed.

1. **FACE PAGE (System Generated)**
   The Face Page is populated automatically with data entered in the online application (applicant’s name, institution, title of application, etc.). The Face Page can be downloaded after completing the application and clicking on the “Validate” button (Proposal Section 9). The Face Page must be signed by the Principal Investigator and Authorized Institutional Official. Co-Principal Investigators, if any, are not expected to sign the Face Page. However, signed letters of collaboration from Co-Principal Investigators should be provided in the Appendix. Scan and email the signed Face Page to awards@cfft.org by the deadline. No hardcopy is required.

2. **BUDGET AND JUSTIFICATION (template available for download)**
   - **Budget Summary**: Complete the summary screen online in Section 6. Up to three (3) years of funding may be requested.
   - **Budget and Justification**: Utilizing the template provided online, please complete and upload a Budget Detail and Justification worksheet for each year of funding being requested.
   - The budget may not exceed $125,000 in direct costs per year (plus 8% indirect costs) for a maximum of three (3) years.

   **Detailed Budget – Direct Costs**
   - **Personnel** - List the name, title/role, institutional salary and percent effort of each staff proposed. Indicate dollar amounts separately for requested salary and fringe benefits. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all sponsors.

   - **Consultant Costs** – Give the name and institutional affiliation of any consultant who has agreed to serve in this capacity, including statisticians and physicians in connection with patient care if they are not listed under personnel. In the budget justification, briefly describe services to be performed, the number of days, rate of compensation, and any other associated costs.

   - **Equipment** - List all items of equipment requested (over $5,000 each), their cost and a brief justification. If funds are requested to purchase equipment that is equivalent to items listed
under Facilities Available, justify the duplication. Indirect costs are not allowable on equipment items.

**Supplies** - Itemize supplies e.g., glassware, chemicals, animals, in separate categories and give the estimated cost of each category.

**Travel** - Describe the purpose of any travel. All travel expenses must comply with the *Cystic Fibrosis Foundation Volunteer/Vendor Expense Reimbursement Policies*. Expenses for travel outside the North American continent are not allowable. Also note that request for travel costs should be limited to no more than $2,000 per person per year, not to exceed $5,000 total in any given year. Travel costs must be detailed per individual. Travel costs for Lung Transplant Consortium Meetings will be reimbursed separately.

**Other Expenses** - Itemize other expenses by major categories, such as duplication costs, publication costs, etc. Justify all items.

**Subcontracts** – The total cost of each subcontract (directs plus indirects) should be listed under “Other Expenses” and included in the applicant’s direct costs. The applicant institution may request indirect costs only on the first $25,000 of each subcontract. Detailed budgets for each subcontract must be provided for each year of support. Negotiations of subcontracts are between the applicant institution and the subcontractor.

**Indirect Costs** – Indirect costs up to 8% are allowable on these awards except for:

- Major equipment (items over $5,000 in value)
- Computer software
- Software licenses

For third party subcontracts, indirect costs may be requested by the applicant on the first $25,000 only of each subcontract.

3. **FACILITIES AVAILABLE** *(template available for download)*

   Use the template available for download on Proposal Central. Describe the facilities and equipment available at the applicant’s institution that will be used for this project, such as laboratory, clinical, animal, computer, office, etc. Provide any additional information about the environment, including any support services available that will be utilized. Describe their pertinent capabilities, proximity and anticipated extent of use. If facilities or equipment at a consultant’s or collaborative site will be used, they should be identified and clearly described. There is no page limit. Use continuation pages, if necessary.

4. **BIOGRAPHICAL SKETCH** *(template available for download)*

   Complete and upload an NIH Biographical Sketch for all key project personnel, beginning with the Applicant/Principal Investigator (fellow). (CFFT defines “key project personnel” as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project.) Do not exceed five (5) pages per person. A sample NIH Biographical Sketch is available for download on Proposal Central.
5. **OTHER SUPPORT** *(template available for download)*

Complete and upload an Other Support form, for all key project personnel, beginning with the Applicant/Principal Investigator. CFFT defines “key project personnel” as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project. There is no page limitation.

6. **RESPONSE TO CRITIQUES** *(template available for download)*

Provide a point-by-point response to the limitations noted in the critiques of the LOI.

7. **CENTER DESCRIPTION AND VISION FOR CONTRIBUTION TO CFLTC** *(template available for download)*

- **Page limit:** (5) single sided pages, not including literature cited. A template is available for download on Proposal Central.

Use up to one page to provide details for review criteria 2 and 3 listed below, Use up to one-half page for responses to criteria 1, 4-7.

**Review Criteria:**

1. Transplant Center qualifications, experience, volume and waitlist details
2. Available research facilities, and previous transplant research experience
3. Narrative describing vision for site’s contribution to CF LTC
4. Ability of Research Staff able to focus on lung transplant research within the CFLTC
5. Experience and volume of lung transplants performed in the last five years for CF
6. Expertise in Lung Transplant Related Specialized research procedures
7. How Institutional environment is supportive of transplant research

Include sufficient information to permit effective review. Information should be presented in a clear and concise manner, while being specific and informative. Key figures and legends must be included in the Center description.

**Literature Cited.** References should be numbered in the sequence that they appear in the text and listed at the end of the Research Plan. Each citation must include the names of authors, the name of the journal or book, volume number, page number and year of publication (titles are optional).

8. **VERIFICATION OF APPLICANT INSTITUTION’S TAX STATUS** *(upload requirements)*

Per Internal Revenue Service (IRS) regulations for grant-making organizations, CFFT’s Grants and Contracts Office must have a copy of the applicant institution’s current W9 and 501(c)3 letter, or other documentation verifying its Federal tax status, on file. CFFT’s Grants and Contracts Office will not issue Award Letters to Grantees if these documents are not on file.

Applicants from for-profit organizations must submit a copy of the applicant institution’s W9 and IRS Form 147C, or other documentation verifying the organization’s Federal tax status. Awards are not issued prior to having these documents on file with the CFFT Grants and Contracts Office.

Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.
9. **INTERNATIONAL INSTITUTION FORM** *(template available for download, upload if applicable)*

Applicants whose sponsoring institution is not based in the United States must complete the International Institution Form. The template is provided for download on Proposal Central. **Upload a PDF version of the completed and signed form, together with the following documents:**

a. A copy of your organization’s most recent Mission Statement.
b. A copy of your organization’s Tax Exemption Letter, if organization is not-for-profit.
c. A description of other sources of support, such as official grants, private endowments, and commercial activities, received by your organization.
d. A copy of your organization’s Standard Operating Procedure(s) or relevant policy to ensure that funds provided are neither distributed to terrorists or their support networks nor used for activities that support terrorism or terrorist organizations.
e. For-profit organizations must submit a complete list of key employees, members of the governing board, and/or other senior management.

English translations must be provided for any documents that are written in the applicant’s or sponsoring institution’s native language, including material provided in support of the Research Plan.

10. **APPENDICES** *(template available for download, upload if applicable)*

- **Up to three documents of the applicant’s work** relating to the general area of research proposed.
- **Letters of support, collaboration, and reference:**
  - If the applicant is not a Transplant Medical Director or Associate Director, a letter of support from the Center Director is **required**.
  - If there are Co-Investigators, a letter of collaboration is **required** from each.
  - Letters of reference (from individuals who are familiar with the applicant’s work in the area proposed in this application) are optional but encouraged.
- **Other materials pertinent to the grant proposal, not already described. Please upload only the most relevant documents, as excessive materials may not be reviewed.**

XIII. **FULL APPLICATION ONLINE SUBMISSION INSTRUCTIONS**

**DEADLINE:** Wednesday November 9, 2016 by 5:00 pm (Eastern)

a. **Log In:** The full application will only be available to applicants who were notified that the LOI submission has been approved. Approval of an LOI will automatically create a full application.

- After logging in be sure to select **Manage Proposals** on the upper right of the screen. Then select **In Progress** toward the upper left of the screen.
- In this screen you will find a list of your In Progress applications. Select the **Edit** button for the Clinical Research Award w/LOI application.

**Start and Continuation:** Application Sections are listed in the gray menu box to the left of the screen. The sections need not be complete sequentially. Click the red **SAVE** button after completing each section.
Enter your project title as “Cystic Fibrosis Lung Transplant Consortium.”

You may stop at any point in the application, each time remembering to SAVE your entries, and return to continue, revise, and upload until you have actually hit the SUBMIT button.

When you log in to continue, click on the blue tab, MANAGE PROPOSALS, and then the Edit button next to your application’s title. Do not start a new application.

b. **Designating Access to Another**: Complete Section 3 online if you wish to designate access to another individual, such as an assistant who has registered on proposalCENTRAL. Enter the full name and email address and in the Permissions column, then use the pulldown menu to select the type of access you wish to give.

c. **Final Steps**

1. **Validate**: Upon completing your application, click on the blue VALIDATE button on the main screen. Attend to any omissions/errors as prompted onscreen, if prompted, and validate again.

2. **Print face page**: After validation, follow the prompts to print the system-generated face page.

3. **Submit**: Click on the gray button with blue lettering. CFFT will not receive your application until and unless you have submitted it. You will receive an email confirmation from proposalCENTRAL (not from CFFT) that your application has been successfully uploaded. This email will be your only acknowledgment. If you do not receive it, please contact proposalCENTRAL immediately to ensure that the application is properly submitted.

4. **Sign, scan and email the face page** to awards@cfft.org by the deadline date, November 9, 2016. The Program Director, as well as the authorized institutional official must sign it. No hard copy is necessary.

---

For technical support with the online application:
Proposal CENTRAL at pcsupport@altum.com or 800-875-2562 on weekdays, 8:00 a.m. to 5:00 p.m. (Eastern)

For program/content information:
CFFT Grants & Contracts at awards@cfft.org or 301-841-2614