Cystic Fibrosis Foundation Therapeutics, Inc.
CLINICAL RESEARCH AWARD
Fall 2016 LOI and Full Application

Policies and Guidelines

CFF Grants and Contracts Office
6931 Arlington Road
Bethesda, MD 20814
(301) 841-2614
awards@cfft.org
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.

Established in 2000, Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) is the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation. CFFT supports and governs activities related to cystic fibrosis (CF) drug discovery through the many stages of drug development and clinical evaluation.

**TABLE OF CONTENTS**

I. AWARD OVERVIEW .................................................................................................................. 3
II. PROGRAM DESCRIPTION ...................................................................................................... 3
III. SUBMISSION INFORMATION & GENERAL TIMELINE ......................................................... 4
IV. REVIEW AND AWARD .......................................................................................................... 4
V. LETTER OF INTENT GUIDELINES ...................................................................................... 5
VI. FULL APPLICATION GUIDELINES ...................................................................................... 7
   A. FACE PAGE ....................................................................................................................... 7
   B. ABSTRACTS (LAY & TECHNICAL) .................................................................................. 7
   C. CRITIQUE RESPONSE* .................................................................................................... 8
   D. BUDGET & JUSTIFICATION* ........................................................................................... 8
   E. FACILITIES AVAILABLE* ................................................................................................ 10
   F. BIOGRAPHICAL SKETCH (NIH FORMAT)* ..................................................................... 10
   G. OTHER SUPPORT (NIH FORMAT)* ................................................................................ 10
   H. RESEARCH PLAN* ........................................................................................................... 10
   I. DATA SAFETY MONITORING PLAN* .............................................................................. 12
   J. VERIFICATION OF APPLICANT INSTITUTION’S TAX STATUS .................................... 13
   K. INTERNATIONAL APPLICANTS* ..................................................................................... 13
   L. ORGANIZATIONAL ASSURANCES & CERTIFICATIONS ............................................. 14
   M. APPENDICES .................................................................................................................. 15
VII. SUBMISSION INSTRUCTIONS .......................................................................................... 16

*A template with instructions or sample is provided online in Section 2 of your LOI/application on ProposalCENTRAL.

A Letter of Intent (LOI) must be submitted and approved prior to submitting a full application.

Online submission at ProposalCENTRAL: [https://proposalcentral.altum.com/](https://proposalcentral.altum.com/)
I. CLINICAL RESEARCH AWARD (CRA) AWARD OVERVIEW

Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT), a non-profit affiliate of Cystic Fibrosis Foundation (CFF), will provide up to $150,000 per year, plus indirect costs of 8%, for up to three years of feasibility support for single center clinical studies; and up to $350,000 per year, plus indirect costs of 8%, for up to three years for multi-center clinical studies. In order to facilitate clinical trials or other larger clinical research initiatives. If your estimated budget exceeds the limitations, please contact CFFT at awards@cfft.org before submission.

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 its arrival, s/he may proceed to the full application. If not approved, a revised LOI may be resubmitted in the next LOI round, provided the applicant address point to point.

II. PROGRAM DESCRIPTION

Clinical research projects must include studies in cystic fibrosis (CF) individuals that are designed to definitively answer some question about the pathophysiology of CF or its management; or planned as pilot and feasibility projects to determine the best strategies and methods for approaching a major question that ultimately will require assessment through larger-scale research and/or multi-center, collaborative trials. For the latter, the ultimate goal and the short-term objectives must be clearly delineated in the application.

Applicants must describe fully the potential impact of the proposed project on the pathological consequences of CF. Limited descriptive projects that are directed towards the formulation of an interventional hypothesis will be considered and, in some cases, encouraged to submit directly to the National Institutes of Health (NIH). The intent of CFFT funding is to provide limited support so that a future award application will be more competitive upon timely resubmission to the NIH.

(CFFT will consider funding larger scope clinical projects that have been submitted to the NIH or to the FDA Orphan Drug Clinical Research Program and have undergone peer review. Unfunded NIH or FDA applications that are of high priority will be considered under the mechanism of CFF/NIH Unfunded grants. Please refer to the information on this program in Grant Opportunities on proposalCENTRAL, listed under Cystic Fibrosis Foundation.)

It is the responsibility of the investigator(s) to develop the underlying hypothesis, rationale, approach and methods for submitted projects, and should thoroughly present these in the application. Applications may be submitted for projects to be undertaken at a single institution or as a collaborative effort amongst a group of institutions. For collaborative efforts amongst institutions, the application should be submitted from the designated lead institution, with other centers as subcontractors.

A clinical trial application must originate from a CFF-accredited CF Care Center. The IRB application must be submitted to the applicant institution BEFORE the CFFT application deadline. Applicants must be able to demonstrate access to a sufficient number of patients and other appropriate subjects based on their CF Care Center’s available subjects, after adjusting for the protocol’s stated inclusion and exclusion criteria. A power analysis that justifies the sample size in the study design must be included (see page 11 section 4). If further data collection is required to estimate the variance of clinical
parameters, it must be described. CFFT requires that a biostatistician be included as a collaborator and consulted during the formulation of this application. CFFT’s plan is to establish an integrated program of clinical research on CF, ranging from investigator-initiated studies to CFFT-organized multi-center collaborative projects. Investigators will be expected to participate in an ongoing, constructive dialogue with the Clinical Research Committee and must submit annual progress reports. Tangible progress must be demonstrated in order for investigators to receive continued funding.

III. SUBMISSION INFORMATION & GENERAL TIMELINE

A Letter of Intent (LOI) must be submitted and approved prior to submitting a full application. Online submission at ProposalCENTRAL: http://proposalcentral.altum.com/

If you have a previously approved LOI (from a prior cycle) you need not submit a new LOI. Request an LOI Bypass.

Applicants whose LOI was not approved in an earlier submission may resubmit the LOI with (1) appropriate revisions and, (2) an attachment that provides a point-by-point response to the limitations noted by the reviewers.

General Timeline:

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOI Deadline</td>
<td>July 18, 2016</td>
</tr>
<tr>
<td>Applicant Notified</td>
<td>mid-August 2016</td>
</tr>
<tr>
<td>Full Application Deadline</td>
<td>October 10, 2016</td>
</tr>
<tr>
<td>Review by Clinical Research Committee</td>
<td>December 2, 2016</td>
</tr>
<tr>
<td>Review by CFFT Board of Directors</td>
<td>February 2017</td>
</tr>
<tr>
<td>Notification to Applicants</td>
<td>late February 2017</td>
</tr>
<tr>
<td>Earliest Start Date for Awarded Projects</td>
<td>April 1, 2017</td>
</tr>
</tbody>
</table>

IV. REVIEW AND AWARD

The CFFT Clinical Research Committee evaluates all applications, and their recommendations are reviewed by the CFFT Executive Board of Directors for final approval and funding. Funding is based on available funds, the priority score awarded each application, and the recommendations of the Clinical Research Committee and the CFFT Board of Directors. All awards are subject to observance of the regulations and policies of CFFT related to that program.

The chief cause of low priority scores assigned to applications include the following:

- Inadequate statement of hypothesis, experimental design, or methods.
- Failure to complete a justification of sample size or estimated power analysis for the study. The Investigator must include estimates and formula used to derive sample size. A biostatistician should be included as a collaborator and consulted during the formulation and writing of the LOI and application.
• Insufficient or improper controls, especially in human clinical studies (e.g. a particular hypothesis may necessitate a control group of individuals with lung diseases other than cystic fibrosis, staging of the severity of lung disease, or age-matched controls).
• Failure to describe potential relevance of the proposed study to clinical issues in cystic fibrosis.
• Failure to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the undertaking, e.g., recruitment of CF patients.
• Failure to document the necessary skills or training to accomplish the goals of the proposal.
• Insufficient information or documentation in proposal, including late or missing letters of reference, IRB.
• Approval; or (for clinical trials) collaboration with CF Care Center staff.
• Failure to adequately describe safeguards for monitoring/ensuring patient safety
• For applications, failure to respond to LOI critiques with a point-by-point discussion of each limitation noted.
• For resubmissions of LOI/application, failure to thoroughly address the concerns and issues raised in the previous review.

V. LOI SUBMISSION GUIDELINES – DEADLINE JULY 18, 2016

Letters of Intent must be submitted online at proposalCENTRAL:
https://proposalcentral.altum.com/

A signed Cover Sheet must be uploaded with the application.

• Font: Times New Roman 12 or Arial 11.
• Margins: No less than a half inch on each side.

If you are a first time user of the online application system at ProposalCENTRAL, register at: https://proposalCENTRAL.altum.com/. If you have registered and cannot remember your password, click on the Forgot Password button.

Grant opportunities, including this, are listed on the opening screen, but you must be logged in first to see the APPLY NOW link appear in the last column on the far right of the screen. Log in, click on the gray Grant Opportunities tab, locate Cystic Fibrosis Foundation Therapeutics and the listing for this program. Click on the Apply Now link to open the application form.

An application will be considered incomplete if it fails to comply with instructions, or if the submitted material is insufficient to permit adequate review. CFFT reviews applications electronically, and only documents submitted online will be reviewed. Late applications will not be accepted, and the deadline will not be waived.

You may stop and exit at any point, each time remembering to SAVE your entries, and return to continue/revise until you have actually hit the SUBMIT button. When you log in again to continue, click on the blue tab, Manage Proposals, and then the Edit button next to your application’s title.

For prompt tech support, please click on the Customer Service link in the top right corner of every screen.
**The Following Sections** are listed in the **gray navigation box to the left of the application screen.**

1. **Title Page:** Complete online. Enter the title of your project, and whether it is a new LOI or a resubmission.

2. **Download Templates & Instructions:** The following are provided to be downloaded, some to be completed offline and uploaded in Section 8.
   a. Instructions
   b. Template: Cover Sheet
   c. Sample: NIH Biographical Sketch
   d. Template: Response to Prior LOI Critique (if resubmission)
   e. Template: Project Description

3. **Enable Other User to Access this Proposal:** Complete this section online to designate access to another individual.

4. **Applicant/PI:** Complete online. Enter PI’s name and address, etc.

5. **Institution and Contacts:** Complete online. Be sure to use the full legal name of the institution.

6. **Scientific & Lay Abstracts:** Complete online or cut and paste plain text (no scientific notations, bold, underline, etc.). Each abstract should be no more than 250 words, up to 2,000-character maximum including spaces. Do not include proprietary or confidential information as these abstracts may be published.
   **Keywords:** From the lists of options provided in this section, select all applicable research type, research topics, and keywords for the proposed project. A minimum of one (1) option must be selected per category. Click each keyword you want to select, then the arrow tab, until you have all applicable keywords selected on the list to the right.

7. **Budget Summary:** All clinical research awards are for a maximum of three years, up to $150,000/year (plus 8% indirect costs) for a single center clinical research award; and up to $350,000/year (plus 8% indirect costs) for a multi-center clinical research award. Rare exceptions may be made, based on merit. If the proposed budget exceeds these amounts, please get prior permission by emailing awards@CFFT.org with “CRA LOI Budget Excess Request” in the subject line, and mark the email urgent to avoid delay.

8. **Attachments:** Complete the templates that you downloaded from Section 2, and upload as PDF’s.
   a. **Biosketches of key personnel:** CFFT defines “key project personnel” as any individual with an advanced degree who will play an instrumental role in the research project. An NIH Biographical Sketch form should be completed for each key project personnel, and uploaded as PDF. The maximum length for each biosketch is four pages. Personnel must include a **biostatistician**, minimum 5% time.
   b. **Cover Sheet:** The Principal Investigator and any Co-Investigators are required to sign where indicated. (The Sponsoring Institution’s Authorized Institutional Official’s signature is not required). Scan and upload.
   c. **Project Description:** Upload a PDF copy of the completed document. Maximum of 3 pages (not including the literature cited). Components should include:
I. Statement of hypothesis

II. Goals of the research

III. Brief study design that must include a detailed power or a sample size analysis on the primary and major secondary analysis. These analyses should include formulas and estimates used to arrive at the sample. An exception to this approach would be a feasibility study where the statistical section should focus on the precision of estimates that will be used to design future studies.

IV. Specific statistical analysis section for the primary and secondary end points.

9. **Validate**: Upon completing your LOI, click on the **VALIDATE** button on the main screen. Attend to any omissions/errors as prompted onscreen, and then click VALIDATE again.

10. **Print Face Page**: Please disregard this section. Face Pages are not required for an LOI. Continue to Section 11.

11. **Submit**: Click on the gray button with blue lettering: Submit CFFT will not receive your application until and unless you have submitted it.

**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 it, please contact proposalCENTRAL immediately to ensure that your submission is processed.

VI. **FULL APPLICATIONS GUIDELINES – DEADLINE OCTOBER 10, 2016**

- Font: Times New Roman 12 or Arial 11.
- Margins: No less than a half inch on each side.

Log-in at ProposalCENTRAL: [https://proposalcentral.altum.com/](https://proposalcentral.altum.com/). If you cannot remember your password, click on the Forgot Password button. Note: The Customer Service link on the top right of each screen to use as need.

You must be logged in first to see the Grant Opportunities listed with the APPLY NOW link in the last column on the far right of the screen. Locate Cystic Fibrosis Foundation Therapeutics and the listing for this program. Click on the Apply Now link to open the application form.

**A. FACE PAGE**

The Face Page will be populated automatically with the application information (applicant’s name, institution, title of application, etc.) entered into the forms online. It will be ready to be printed as one of the final steps of the application. The Applicant (or Principal Investigator) and Signing Official authorized to sign on behalf of the Sponsoring Institution are both required to sign where indicated on the Face Page. Only these two signatures are required. Co-Investigators’ signatures are not required. Scan and email the signed Face Page to awards@CFFT.org by the deadline date.

**B. ABSTRACTS** (complete online)

Provide a Lay Abstract and a Scientific Abstract, no more than 250 words each, 2000 characters including spaces, to summarize your proposal and its relationship to CF. The lay abstract will be used to inform the non-scientific departments of CFFT and the general public. The scientific abstract will
be used for the scientific community. Do not include proprietary or confidential material. In the boxes below, select all applicable research topics and keywords.

C. CRITIQUE RESPONSES (template available for download)
For new applications: Provide a point-by-point response to the limitations noted in the critiques of the LOI, using the template provided online.

For resubmissions of revised applications: Provide a point-by-point response to the prior reviews.

D. BUDGET AND JUSTIFICATION
• Budget Summary: Complete online in Section 7. Up to three (3) years of funding may be requested.
• Budget and Justification: Upload the complete template.

For a single center project, the budget may not exceed $150,000 in direct costs per year (plus 8% indirect costs) for a maximum of three (3) years.

For a multi-center project, the budget may not exceed $350,000 per year in direct costs (plus 8% indirect costs) for a maximum of three years.

If the estimated budget for a proposal exceeds these limitations, email awards@CFFT.org before submission.

Please write “CRA Application Budget Request” in the subject line and mark it urgent to avoid delay.

1. Budget Guidelines
• Services that are part of routine medical care may not be included in the project budget. Whenever possible, the price of services (e.g., X-rays, EKGs, PFTs, etc.) provided by the institution should be negotiated to the lowest possible non-profit price.
• Separate professional fees for interpretation of data (e.g., from X-rays, lab tests, PFTs) may not be included when such interpretation is performed by the named investigator(s), co-investigator(s), or consultants as part of the project, other than in exceptional circumstances. In such cases, justification for these fees must be described in detail.
• Under most circumstances, hospitalization costs of study subjects cannot be included in this budget.

2. Detailed Budget – Direct Costs
Personnel – List the names and positions of all professional and non-professional personnel involved in the project, whether or not salaries are requested. Indicate the percent of time or effort per week on the project for professional personnel; indicate the hours per week for each non-professional. For each individual, list dollar amounts separately for salary and fringe benefits.

In accordance with National Institutes of Health (NIH) policy, the institutional base salary of an individual should not exceed the current federal salary cap of $185,100. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all
sponsors. The percentage of salary requested cannot exceed the percent effort for each professional and non-professional personnel. Note that a biostatistician is required for all projects, at a minimum of 5%-time effort.

**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. Under budget justification, briefly describe services to be performed, the number of days, rate of compensation, per diem and any other associated costs.

**Equipment** - List all items of equipment requested and the cost of each. If funds are requested to purchase equipment that is equivalent to items listed under Facilities Available, justify the duplication. Justify any item of equipment for which the need may not be obvious.

**Supplies** - Itemize supplies, such as glassware, chemicals, animals, etc., in separate categories and give the estimated cost of each category. If animals are involved, state the number, unit purchase cost, and unit care cost.

**Travel** - In addition, up to **$2,000 per year** may be requested for travel. Travel outside the North American continent, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable expenses.

**Patient Care Costs** - Funds may be requested for patient care costs specifically related to the proposed research. The basis for estimating funds requested in this category should be justified. The scientific need for patient care costs will be considered in the review. Please note that patient travel, lodging, and sustenance should be listed in "Other Expenses;" and consulting physician charges should be listed under "Consultant Costs."

**Other Expenses** - Itemize other expenses by major categories, such as subcontracts, duplication costs, publication costs, computer charges, equipment maintenance, 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. 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 of 8% may be applied to subcontracts, but only on the first $25,000 of each subcontract.

3. **Budget Detail**
   Indirect Costs of 8% may be requested, 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.
4. **Budget Justification**
   Describe and justify the Line items in the Detailed Budget in terms of major categories, such as Personnel, Consultant Costs, Equipment, etc.

E. **FACILITIES AVAILABLE (template available for download)**
   Describe the facilities and equipment available at the applicant’s organization that will be used for this project.
   - 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. Use continuation pages, if necessary.
   - Relevant areas, such as laboratory, clinical, animal, computer, office. Provide any additional information about the environment, including support services available to be utilized for this project.

F. **BIOGRAPHICAL SKETCHES (template available for download)**
   Provide an NIH Biographical Sketch (the current or older version) for each of the key personnel, beginning with the Principal Investigator. CF is 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. Clearly identify the results of past CFF/CFFT support (i.e. subsequent funding from other sources, journal articles, and invited presentations).

G. **OTHER SUPPORT (template available for download)**
   List all other support that all key project personnel are currently receiving. There is no page limitation for this. Use NIH Other Support Format Pages. A sample is available for download on ProposalCENTRAL.

H. **RESEARCH PLAN (template available for download)**
   - Maximum 12 pages, not including the Literature Cited
   - Number the pages at the bottom, and write the PI’s name at the top of the page.
   
   The Research Plan for full applications is limited in length to 12 single-sided pages, plus the Literature Cited. Applications that exceed this page limit or circumvent it by placing critical data into the Appendix will not be reviewed. Include sufficient information to permit effective review without reference to previous applications. The plan should be clear, concise, specific and informative. Key figures and legends must be included in the document.

   If this application is a resubmission of an earlier proposal, the changes should be clearly indicated by a change in the typeface, underlining, or marks in the margins. Unchanged protocols will not be reviewed.

   1. **Hypotheses and Specific Aims (1 page):** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. Do not exceed one page. The focus of applications should be aligned with the mission of the Cystic Fibrosis Foundation (CFF): 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.
2. **Background and Significance (maximum 3 pages):** Briefly describe the background of the present proposal. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this research by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF. In addition, the applicant should describe the relationship of the proposed work to his/her long-term career goals. Preference will be given to those applicants who have an interest in a long-term career in CF-related research.

3. **Preliminary Studies (maximum 8 pages):** Summarize any preliminary work pertinent to this application that has been undertaken by the Principal Investigator(s) and/or information that will establish the competence and/or experience of the investigator(s) to pursue the proposed study. Titles, complete references and supplemental charts, graphs, etc., may be submitted in the Appendix.

4. **Experimental Design and Methods:** Provide a detailed discussion of the experimental design and procedures to be used to accomplish specific aims. Please discuss: study hypothesis; primary and secondary outcome measures; study design; study sample-inclusion and exclusion criteria; sample size estimates;* subject enrollment including age range; puberty status; gender distribution; randomization scheme if applicable; description of experimental procedures and schedule including a study time-line; drugs and dosage; measures of compliance; follow-up schedule including a time-line for full project up to three years; ascertainment of response variables: efficacy and safety, training, data collection, data monitoring and quality control; and a description of your proposed data analysis and statistical procedures for your hypothesis testing. Although no page limit is specified for this section, make every attempt to be concise and succinct.

*For sample size estimates,* please provide all estimates of means, standard deviations, rates or proportions used to calculate each of your sample size or power estimates. Please include in the statistical section whether you will use a one or two-tailed test, the power selected for such a test (if making a sample size calculation), and the reference for your sample size or power calculation. In instances of pilot studies where some of these parameters are unknown, we will accept your best estimates of the unknown parameters if preliminary data are not available, and if your calculation is a preliminary estimate before formal sample size can be calculated for a larger study. Please identify if you are making estimates from data or from personal estimates. This section must document access to adequate numbers of subjects. The number of CF patients in the participating CF Center(s), as well as the number in relevant control groups, must be specified. Discuss the potential difficulties and limitations of the proposed procedures and alternative strategies for achieving the aims. Please provide a copy of your institution’s IRB approval and/or protocol with proposed patient consent forms.

5. **Consultant Arrangements:** If the proposed project includes consultant arrangements and/or collaboration with other individuals outside the applicant's group, describe the working relationships and support this description by letter(s) of intent signed by collaborating individual(s). If clinical material required by this grant is to be furnished by other individuals, include a statement from these individuals agreeing to their participation and precautions taken to ensure anonymity of patients.
6. **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).

I. **DATA SAFETY MONITORING PLAN (template available for download)**

In compliance with Federal regulations, all applicants must submit a general description of the Data Safety Monitoring Plan (DSMP) for any proposed study that places human subjects at more than minimal risk. A DSMP helps to ensure subject safety, as well the validity and integrity of the data. Furthermore, a DSMP allows for the monitoring of study data to assess whether or not an early termination is necessary for safety or efficacy reasons.

The extent of monitoring required for a study is dependent on the level of risk involved for the subjects, as well as the size and complexity of the study. CFFT-funded Phase III clinical trials must utilize a Data Safety and Monitoring Board (DSMB). In addition, CFFT recommends that investigators utilize a DSMB for any Phase I or II clinical trials that are:

- Multi-center;
- Blinded to the investigator;
- Conducted in an emergency setting;
- Use high-risk interventions, such as gene therapy or gene transfer; or
- Include particularly vulnerable study populations, such as pediatric patients.

**Address the following areas in the DSMP:**

**Assessment of Risk** – Describe the level of risk the proposed research presents to subject participants and provide a detailed justification for the level of risk. Discuss who will monitor the study.

**Level of Risk**

- **Minimal Risk**
  - Study poses no more risk than expected in daily life (blood draw, physical exam, etc.)
  - Observational studies
  - Survey or questionnaire studies
- **Low Risk**
  - Post-marketing study Phase IV drug or device, as defined by FDA
- **Moderate Risk**
  - Substantial risk (>5%) of a Serious Adverse Event (SAE) originating from the underlying condition of the enrolled subject
  - Phase I or II study with available safety data in humans
  - High Risk
  - Involves an intervention or invasive procedure with
substantial risk
  o Involves the use of a new chemical or drug for which there is little or no toxicology data in humans
  o A gene therapy study or research involving recombinant DNA molecules (gene transfer)
  o Involves vulnerable populations (pediatric, pregnant, etc.)

Anticipated Adverse Events and Grading Scale – Describe anticipated adverse events (AEs), including expected frequency and the grading scale to be used. Discuss plans for addressing AEs.

Reporting of AEs – Detail the plan for reporting AEs, including who shall be notified in the event an AE should occur.

Safety Monitoring Plan – Describe all tests, evaluations, and exclusion criteria that will be implemented to ensure and monitor the safety of human subjects. Discuss plans for stopping the study if necessary.

Safety Reviews – Describe the process for monitoring and reviewing subject safety data, including the frequency of such reviews. Include details as to who will perform the monitoring and plans for reporting. If utilizing a DSMB, provide a composition of the board, the functions of the board, the frequency of meetings, the reporting requirements, including AEs, and the procedure for interim reporting as necessary.

J. VERIFICATION OF APPLICANT INSTITUTION’S TAX STATUS
Per internal Revenue Service (IRS) stipulations 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.

K. INTERNATIONAL INSTITUTION FORM (template available for download)
Applicants whose sponsoring institution is not a United States based entity 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 copy of your organization’s most recent Mission Statement.
  • A copy of your organization’s Tax Exemption Letter, if organization is not-for-profit.
A description of other sources of support, such as official grants, private endowments, and commercial activities, received by your organization.

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.

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.

L. ORGANIZATION ASSURANCES & CERTIFICATIONS

Research Involving Human Subjects: CFFT policy pertaining to the protection of individuals as research subjects requires that for each proposal submitted, the applicant institution certify in writing that an Institutional Review Board (IRB) has reviewed and approved the procedures for the use of human subjects, or human organs, tissues and body fluids, in the proposed research, in accordance with Department of Health and Human Services policies. This certification should accompany the application and must be received before activation of any grant. If approval does not accompany the application, there should be a statement in the application indicating that such approval is pending and the date when such approval is expected. The IRB application must be submitted to the applicant institution BEFORE the CFFT application deadline.

Research Involving Recombinant DNA: All research involving recombinant deoxyribonucleic acid (DNA) techniques and human gene transfer supported by CFFT must meet the requirements contained in the document NIH Guidelines for Research Involving Recombinant DNA Molecules (revised May 2011). This publication and announcements of modifications and changes to the NIH Guidelines are available from the Office of Biotechnology Activities, National Institutes of Health, 6705 Rockledge Drive, Ste 750, MSC 7985, Bethesda, MD, 20892-7985 or on-line at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.

The purpose of the NIH Guidelines is to specify practices for the construction and handling of: (i) recombinant deoxyribonucleic acid (DNA) molecules, and (ii) organisms and viruses containing recombinant DNA molecules. As defined by the NIH Guidelines, recombinant DNA molecules are either: (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell; or (ii) molecules that result from the replication of those described in (i) above.

Many types of studies involving recombinant DNA are exempt from the NIH Guidelines while others are prohibited. The applicant organization is required to establish and implement policies that provide for the safe conduct of the research in full conformity with the NIH Guidelines. This responsibility includes establishing an Institutional Biosafety Committee to review all recombinant DNA research to be conducted at or sponsored by the applicant organization, and to approve those projects it finds are in conformity with the Guidelines.

CFFT policy pertaining to recombinant DNA research requires that the applicant institution certify in writing that an institutional committee has reviewed and approved the procedures involving recombinant DNA in accordance with the NIH Guidelines. Applicants that do not have
institutional committee approval must submit a recombinant DNA application to the applicant institution BEFORE the CFFT application deadline. Certifications do not need to accompany the application; however, applicants must provide copies of all required certifications upon request by CFFT.

Research Involving Animals: Grant applications submitted to CFFT involving the use of animals must meet the guidelines of the National Institutes of Health, U.S. Public Health Service, which require that all proposed studies be reviewed and approved by an Institutional Animal Care and Use Committee (IACUC). In addition, CFFT grantee institutions and laboratories must be accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and/or have other verifiable assurances that the institution and laboratory meet appropriate standards. Applicants that do not have institutional committee approval must submit an IACUC application to the applicant institution BEFORE the CFFT application deadline. Certifications do not need to accompany the application; however, applicants must provide copies of all required certifications upon request by CFFT.

M. APPENDICES

- **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 CF Center Director or Co-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.

- **IRB Application and Informed Consent Documents**

- Other materials pertinent to the grant proposal, not already described. Please upload only the most relevant documents, as excessive materials may not be reviewed.
VII. SUBMISSION INSTRUCTIONS

Application Deadline **OCTOBER 10, 2016 by 5:00 PM EST.**

Applications must be submitted at ProposalCENTRAL: [https://proposalcentral.altum.com/](https://proposalcentral.altum.com/).

A PDF copy of the signed, Face Page should be emailed to CFFT at awards@cfft.org on the same day as the electronic submission. Late applications will not be accepted and the deadline will not be waived. CFFT reviews applications electronically; therefore, anything not submitted online will

Register at ProposalCENTRAL if you have not already done so. If you have registered already, and cannot remember your password, click on the Forgot Password button.

The opening screen, after logging in to Proposal Central, includes multiple grant opportunities organized by Grant Maker and Program. If this screen does not appear, click on the gray tab labeled “Grant Opportunities” found on the upper right hand side of the page. Scroll down to **Cystic Fibrosis Foundation Therapeutics, Inc.** and click on the “Apply Now” button that appears on the far right next to the program name, “**Clinical Research Award**,” to begin.

Instructions and templates are provided for review/download in related sections of the application. If you need tech support, please use the contact information that is provided on each screen.

Applicants may stop at any point, each time remembering to click the SAVE button before exiting, and continue/revise until clicking on the SUBMIT button. When logging in to continue, click on the blue tab, “Manage Proposals,” and then the Edit button next to the application’s title.

Access may be designated to another registered individual, such as an assistant, in Section 3, “Enable Other Users to Access This Proposal.” Enter the designated individual’s full name and email address, and in the Permissions column select the type of access allowed from the drop-down menu.

An application will be considered incomplete if it fails to comply with the instructions, or if the submitted material is insufficient to permit adequate review. CFF reviews applications electronically, and only documents submitted online at Proposal Central will be reviewed. Late applications will not be accepted, and the deadline will not be waived.

Upon validating your application, follow the prompts to print the system-generated face page. Please hit the SUBMIT button to complete the application process. Sign, scan and email the Face Page to awards@cfft.org by the deadline date.

An email confirming successful upload will be sent from Proposal Central, not CFFT. This will be the only acknowledgement that the application was successfully uploaded. If this acknowledgement is not received, contact Proposal Central for assistance.
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