



# **Advancing Gene Editing Technologies and Tools for Cystic Fibrosis: Collaborative Research Grant**

## **POLICIES AND GUIDELINES**

**Published: November 9, 2018**

**Application Deadline: March 12, 2019**

## **I. ABOUT THE CYSTIC FIBROSIS FOUNDATION**

The mission of the Cystic Fibrosis Foundation (CFF) is to cure Cystic Fibrosis (CF) and to provide all people with the disease the opportunity to lead full, productive lives by funding research and therapeutic development, promoting individualized treatment, and ensuring access to high-quality, specialized care.

To achieve this mission, various types of awards are offered to support meritorious research in CF.

## **II. BACKGROUND**

Cystic Fibrosis is a common, lethal autosomal recessive disorder that affects 70,000 individuals worldwide. Abnormal mucus production in the respiratory tract is the primary cause of morbidity and mortality in CF, but other organs are also affected including the pancreas, sweat gland, intestine, bile duct of the liver, and male reproductive system. CF is caused by dysfunction of a single gene, Cystic Fibrosis transmembrane Conductance Regulator (CFTR), which codes for an ABC transporter protein that functions as a plasma membrane anion channel in epithelial and other cells.

Close to 2,000 variants of CFTR have been identified, however a single mutation, F508del (a 3bp deletion causing absence of phenylalanine 508) is present in ~90% of patients worldwide. The F508del mutation causes instability of CFTR leading to a misfolded protein and defective chloride channel function. Clinical development of small molecule CFTR modulators that reverse the folding defect holds promise for new therapies for the majority of CF patients.

However, there is still an unmet need for patients with CFTR mutations that do not yield sufficient quantities of protein for pharmacological correction. To treat all patients with CF, it will be necessary to correct variants that block protein synthesis (i.e. premature stop codon mutations, splice mutations, insertion/deletion mutations etc.). Gene repair or insertion strategies, as well as overcoming hurdles of poor delivery and cellular penetration, are issues to be addressed.

## **III. COLLABORATIVE PROGRAM RESEARCH GRANT AWARD OVERVIEW**

As an outcome of a CF gene editing workshop held over the summer, the Cystic Fibrosis Foundation announces a Request for Applications (RFA) to identify and support highly meritorious proposals in gene editing that offer potential to repair or circumvent CFTR mutations in individuals with CF. A key concept that emerged from the workshop was that investigators without experience in CF research would be more inclined to become involved if access to CF tools and reagents, as well as CF knowledge, were available. To bring new technologies to the CF field, investigators without experience in CF research are encouraged to apply. Information about CF resources may be found at <https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/>. Additional questions may be directed to [grants@cff.org](mailto:grants@cff.org).

Collaborative, synergistic projects are considered particularly valuable when bringing together investigators with complementary expertise to facilitate development and application of editing strategies. (A description of “Collaborative Program” is found later in this section of the RFA.)

**Note:** A summary of the CF Gene Editing summer workshop can be found within the application on proposalCENTRAL as an informational download document in Section #2.

**Proposals will focus on exploring technologies related to gene editing and generating tools for assessing editing. These include, but are not limited to, studies aimed at:**

- Creating tools, including animal models, cell lines or organoids, that will be generally applicable and facilitate or accelerate development and assessment of various gene editing strategies
- Developing and optimizing novel gene editing technology platforms and strategies to target the CFTR gene locus.
- Improving our understanding of potential effects of *CFTR* gene editing on gene and chromatin topology as related to regulation of *CFTR* expression.
- Developing and applying assays to assess off-target effects and adverse events of *CFTR* gene editing *in vitro* and/or *in vivo*.
- Developing biological endpoints and assays for early *in vivo* efficacy signals of *CFTR* gene editing.
- Understanding and developing assays to monitor potential immune responses to gene editing. This may include responses to the delivery vehicle, cargo, or CFTR protein.
- Utilizing CF and/or non-CF animal models to address optimal delivery approaches, appropriate cell targets for long-term correction, dosing, safety, and phenotypic correction of CF pathology.
- Identifying the threshold of *CFTR* gene editing needed to reach therapeutic relevance.
- Identifying and overcoming barriers for delivery of gene editing cargo into cells relevant to CF.

**General Guidelines and Eligibility:**

- Funding limits are up to **US\$750,000** per year for collaborative research efforts (maximum **US\$250,000** per project per year within the collaborative project) for up to three (3) years. Up to **US\$25,000** additional funds may be may be requested for administrative support of multi-project programs, with justification, plus eight percent (8%) indirect costs.
- U.S. residents and applicants from outside the U.S. are welcome to apply.
- International applicants and institutions are required to submit additional information in accordance with U.S. anti-terrorism restrictions.
- Applicants must be independent investigators:
  - Must be a M.D., Ph.D. or dual M.D., Ph.D. and must be a well-established scientist.
  - Must demonstrate a track record of discovery, investigation, and external funding resulting into long-term commitment of salary, personnel and research resources.
  - Funding available for non-profit and for-profit institutions/organizations

**Collaborative Program Description:**

The objective of the Collaborative Program is to support an integrated, multi-investigator collaborative research program project with a well-defined, central focus related to technology development for gene editing. A single collaborative program can include up to three related research projects that share a well-defined collaborative theme, focus, and/or overall objective.

Each project supported through this mechanism should contribute to a common unifying theme or focus of the entire Collaborative Program Project. Each individual research project should reflect an individual scientifically meritorious research effort. However, the individual research projects should be clearly interrelated and synergistic so that the outcomes of the Collaborative Program will offer a distinct advantage over pursuing the individual research projects separately. Collaborative Programs may include multiple investigators at the same institution. However, multi-institution collaborations are encouraged and will be prioritized.

A plan for ongoing and regular communication, nature of the collaboration, and sharing of reagents and data is required. Consultant arrangements or outside collaborations are also allowed and should be justified.

One application is required for all collaborative projects. One PI must submit the application on behalf of all participating collaborators. Each project that is part of the collaborative program project (grant) must provide an independent budget and budget justification, as part of a single application (see pC guidance).

The lead site for the collaborative program project grant is eligible for administrative support, up to **US\$25,000** direct cost. The administrative budget is designed to help support the day-to-day activities across the program project, communications among project and core leaders, contractual activities (if any), and other overall program project activities, such as leadership meetings

For consultant arrangements with investigators outside the applicant's or Collaborative Program's group, letter(s) of support should be included, a description of the working relationship, and a communication/data sharing plan.

#### **IV. RESEARCH AREAS OF INTEREST TO ADVANCING GENE EDITING TECHNOLOGIES AND TOOLS FOR CYSTIC FIBROSIS**

Cystic Fibrosis is a common, lethal autosomal recessive disorder that affects 70,000 individuals worldwide. Abnormal mucus production in the respiratory tract is the primary cause of morbidity and mortality in CF, but other organs are also affected including the pancreas, sweat gland, intestine, bile duct of the liver, and male reproductive system. CF is caused by dysfunction of a single gene, *Cystic Fibrosis Transmembrane conductance Regulator* (CFTR), which codes for an ABC transporter protein that functions as a plasma membrane anion channel in numerous cell types.

Clinical development of small molecule CFTR modulators that reverse the folding defect of the most common CFTR mutation, F508del (a 3bp deletion causing absence of phenylalanine 508), holds promise for new therapies for the majority of CF patients. However, there is still an unmet need for patients with CFTR mutations that do not yield sufficient quantities of protein for pharmacological correction. To treat all patients with cystic fibrosis, it will be necessary to correct variants that block protein synthesis (i.e. premature stop codon mutations, splice mutations, insertion/deletion mutations etc.). Gene repair strategies as well as overcoming hurdles of poor delivery and cellular penetration are issues that need to be addressed.

It is anticipated that many applicants with relevant technologies in editing and delivery, for example, will not have a history in CF research, and such applications are strongly encouraged.

**Areas of interest with high priority that focus on exploring technologies related to gene editing and generating tools for assessing editing include:**

- Creating tools, including animal models, cell lines or organoids, that will be generally applicable and facilitate or accelerate development and assessment of various gene editing strategies
- Developing and optimizing novel gene editing technology platforms and strategies to target the CFTR gene locus.
- Improving our understanding of potential effects of CFTR gene editing on gene and chromatin topology and the effects on regulation of CFTR expression.
- Developing and applying assays to assess off-target effects and adverse events of CFTR gene editing in vitro and/or in vivo.
- Developing biological endpoints and assays for early in vivo efficacy signals of CFTR gene editing.
- Understanding and developing assays to monitor potential immune responses to gene editing. This may include responses to the delivery vehicle, cargo, or CFTR protein.
- Utilizing CF and/or non-CF animal models to address optimal delivery approaches, appropriate cell targets for long-term correction, dosing, safety, and phenotypic correction of CF pathology.
- Identifying the threshold of CFTR gene editing needed to reach therapeutic relevance.
- Identifying and overcoming barriers for delivery of gene editing cargo into cells relevant to CF.

**V. REVIEW AND AWARD**

All applications are evaluated by a CFF ad-hoc review committee. Funding of awards is based on the priority score awarded to each application and the recommendations of the committee and CFF. Funding decisions are based on the relevance of the proposed study to the goals of the RFA and the mission of the CF Foundation. All awards are subject to compliance with applicable regulations and CFF policies and are contingent upon the availability of CFF funds.

**Collaborative Project Applications will be evaluated on the following:**

- Responsiveness to the RFA, relevance to one or more of the following priority areas:
  - Editing platform development
  - Animal, cell and/or organoid model development for testing editing
  - Animal model testing
  - Delivery system development or testing
  - Safety/adverse events of editing
  - Immune responses
  - Other
- Scientific merit of individual projects as described in the applicant's Research Plan
- PI's/PIs' background and experience
- Adequate site facilities and resources for the project
- How an individual applicant fits within the larger collaboration
- Value added (synergy) from the collaboration

- How the individual applicants will communicate and collaborate (e.g. sharing reagents and data)

**Chief causes for assigning low priority scores to applications during review include the following:**

- Unresponsiveness to the RFA
- Lack of synergy demonstrated among collaborative investigators
- Insufficient information or documentation
- Inadequate statement of experimental design or methods
- Failure of the applicant to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the proposed research
- Insufficient or improper controls
- Failure of the applicant to document the necessary skills or training to accomplish the goals of the proposal
- Failure of the applicant to meet all the criteria described in the policy statement for a given award

## VI. SUBMISSION INFORMATION AND GENERAL TIMELINE

**Application Deadline: Tuesday, March 12, 2019 at 5:00 PM (ET)**

Submit online through proposalCENTRAL: <https://proposalcentral.altum.com/>  
(Refer to Section VII of these guidelines for specific submission instructions.)

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 proposalCENTRAL will be reviewed. Late applications will not be accepted, and the deadline will not be waived.

### General Timeline:

Application Deadline _____	March 12, 2019
Review by committee _____	mid-May 2019
Notification to Applicants _____	late-May 2019
Earliest Start Date for Awarded Projects _____	July 1, 2019

## VII. FULL APPLICATION GUIDELINES

Applications must be submitted online at proposalCENTRAL: <https://proposalcentral.altum.com/>

### Documents should be typed using:

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

**Note:** *When all the documents have been uploaded to proposalCENTRAL, the system will compile them into a single PDF file in the correct sequence.*

Log-in at proposalCENTRAL: <https://proposalcentral.altum.com/>

First-time applicants must register to create a user name and password for proposalCENTRAL and will need to complete a profile online before applying. If you are registered and cannot remember your password, click on the “**Forgot Your Username/Password?**” link below the “**Application Login**” fields.

Award opportunities, including this Request for Applications (RFA), are listed on the opening screen, but you must be logged in first to see them.

Select the gray tab labeled “**Grant Opportunities**” found in the upper right-hand side of the page.

Click on the light blue “**Filter by Grant Maker**” button to the left and scroll down to locate Cystic Fibrosis Foundation in the list.

Locate the listing for the “**Advancing Gene Editing Technologies and Tools for CF: Collaborative Research Grant**” program. Click on the “**Apply Now**” button in the column on the far right to open the application form.

Applicants may stop at any point but must click the “**Save**” button before exiting in order to save their work. When logging in to continue, click on the blue tab, “**Proposals**”, and then the “**Edit**” button.

The following sections are listed in the navigation menu to the left of the application screen. Click on each section and follow the directions:

- 1. Title Page:** Enter the title of your project, and indicate whether the Principal Investigator (PI) is an investigator new to CF.
- 2. Download Templates & Instructions:** Download the available templates applicable to the project, fill them out and upload them when completed in Section #9. Templates available include: CF Gene Editing Workshop Summary (for reference purposes only), Biographical Sketches of Key Personnel, Results of Past and Current CFF/CFFT Support, Other Support, Facilities Available, Budget Detail, Budget Justification, Research Plan, Collaborative Program Description, and International Institution Form.
- 3. Enable Other User to Access this Proposal:** Complete this section online if you wish to designate access to another individual, such as an assistant such as an assistant who has registered on proposalCENTRAL. Enter the email address of the individual and in the “**Permissions**” column, use the pulldown menu to select the type of access you wish to give. Please note that only delegates who are granted “**Administrator**” rights can submit applications on behalf of the applicant. Check the “**Auto Notify**” box and then “**Save**”.

- 4. Applicant/PI:** If a profile was completed upon registration, the fields in this section will already be populated with the information entered in your Professional Profile. If you need to make any changes, click the “**Edit Professional Profile**” button and follow the instructions. If a profile was not completed, enter the required information and click “**Save**”.
- 5. Institution & Contacts:** If a profile was completed upon registration, the Principal Investigator’s (PI) institution will be preloaded as Lead Institution. If a profile was not completed, enter the required information and click “**Save**”. Be sure to use the full legal name of the institution.
- 6. Abstracts/Relevance/Responsiveness:** In the space provided online for abstracts, provide a statement of no more than 2,000 characters (including spaces) explaining the subject of the research proposal and its relationship to CF. Two different abstracts are required, as follows:
- **Lay Abstract:** This statement will be used to inform the non-scientific departments of CFF and the general public of the nature of this work. Applicants should not include any confidential or proprietary information, including intellectual property, in the lay abstract.
  - **Scientific Abstract:** This statement will be used to inform the scientific community.
  - **Summary of Relevance to CFF mission and RFA:**  
All applications are reviewed and scored not only on scientific merit but also on relevance to CFF’s mission and RFA objectives:
    - **Mission:**  
*The mission of the Cystic Fibrosis Foundation 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.*
    - **RFA objectives:**  
*The objectives of the Advancing Gene Editing Technologies and Tools for Cystic Fibrosis RFA are to develop, optimize and apply gene editing technologies to the CFTR locus and generate tools to assess editing efficiency, functional outcome, and potential off-target effects.*

Provide a statement of no more than 2,000 characters (including spaces) summarizing the relevance of the proposed research, for a scientific audience who may or may not have a background in the subspecialty of the proposed research.

- **Responsiveness to this RFA:** From the lists of options provided in this section, select all applicable areas of interest for the proposed project. A minimum of one (1) option must be selected per category. Click each area you want to select, the “Add (+) icon”, until you have all applicable keywords selected on the list to the right. If selecting Other, please indicate the area of interest of the proposal.

- 7. Budget Summary:** Fill in the start and end date and applicable amounts for each year of support requested by completing the online fields (Period 1, 2). All Collaborative Program Research Grants are for a maximum of three years. The total budget requested per project within the collaborative research effort cannot exceed **US\$250,000** per year plus 8% indirect costs. The cumulative total budget for a Collaborative Program may not exceed **US\$750,000** per year. The lead site for the Collaborative Program may request up to an additional **US\$25,000** for administrative expenses with proper justification. *Note: The Budget Detail and Budget Justification templates downloaded in Section #2 need to be completed and uploaded in Section #10 for each year of the award and for each project or subcontract (if applicable). The amounts included in this uploaded Budget Detail must match the amounts entered in the Budget Summary online.*
- 8. Organization Assurances:** Select the type of assurances that are applicable to the project and provide all required information (i.e. IRB, IACUC, and/or IBC/rDNA approval letter and status at the time of submitting the application). Refer to Section K. ORGANIZATION ASSURANCES & CERTIFICATIONS in these guidelines for details.
- 9. Research Plan & Supporting Documents:** In this section, upload the completed templates downloaded in Section #2 above in PDF format. Fill out the fields describing the attachment, select the attachment type from the pulldown menu, enter a description for the attachment in the corresponding field, choose the file to be uploaded, and drag and drop it as indicated in the online form. Click **“Upload and Continue”**. Do this for each attachment. Click the **“Back”** button when all required files have been uploaded to go back to the main screen.
- A. BIOGRAPHICAL SKETCHES OF KEY PERSONNEL (template available for download)**  
Complete and upload an NIH Biographical Sketch for all key project personnel, beginning with the Applicant/Principal Investigator. International applicants can upload a biosketch that is equivalent in content to the NIH template provided. (CFF defines “key 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.
- B. RESULTS OF PAST AND CURRENT CFF/CFPT SUPPORT (template available for download)**  
The Principal Investigator (PI) and any Co-Principal Investigator(s) (Co-PIs) if applicable, are requested to identify the results of past and current Cystic Fibrosis Foundation (CFF) or Cystic Fibrosis Foundation Therapeutics, Inc. (CFPT) support (e.g. subsequent funding from other sources, journal articles, and invited presentations), and the CFF/CFPT award from which they resulted for the past five (5) years. Please note that the following information must be included with each research project identified:
- CFF/CFPT Award #
  - Principal Investigator (PI)
  - CFF/CFPT Project Title
  - Applicant’s Title on Project
  - Project Start/End Dates
  - Total CFF/CFPT Award Amount

- Results of Support

**C. OTHER SUPPORT (template available for download)**

Complete and upload the “Other Support” form for all key project personnel, beginning with the Applicant/Principal Investigator. There is no page limitation. Information on other support assists CFF in the identification and resolution of potential sources of overlap. Scientific and budgetary overlap should be minimized. Commitment of an individual’s effort greater than 100 percent, is not permitted.

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

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.

**E. BUDGET DETAIL AND BUDGET JUSTIFICATION (separate templates available for download)**

Fill out the Budget Detail and Budget Justification templates for each an all years of support requested. In the space provided on the templates, indicate the year or period as well as the start and end dates for the proposed budget period. Each project or subcontract within the program requires a separate Budget Detail and Budget Justification. Be sure the amounts entered in the Budget Detail(s) match the entered in the online budget summary in Section #7).

- **Budget Detail – 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 effort on the project for all personnel. For each individual, be sure to complete all fields on the Budget Detail in full on the template provided. In accordance with National Institutes of Health (NIH) policy, salary requests may not use an institutional base salary in excess of the current federal salary cap of US\$189,600. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all funding agencies and foundations.

**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 the project if they are not listed under personnel. In the 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 greater than US\$5,000 requested and the cost of each item. 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 e.g. glassware, chemicals, animals, 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** - Describe the purpose of any CF-relevant travel. Please note: expenses for travel outside the North American Continent, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable expenses without prior written approval from the CFF Grants and Contracts Office. Travel expenses may not exceed US\$1,250 per person per year. Registration fees associated with conferences are in addition to this allowance should be listed under “Other Expenses”.

**Other Expenses** - Itemize other expenses by major categories, such as subcontracts, duplication costs, publication costs, computer charges, etc. Tuition costs may be requested for personnel supported through this study but may not exceed US\$10,000 per person per year.

**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 and justifications must be provided for each subcontract for each year of support (if applicable, complete a Budget Detail and Budget Justification template for each subcontract). Negotiations of subcontracts are between the applicant institution and the subcontractor.

- **Budget Detail – Indirect Costs**

Indirect costs of up to eight percent (8%) may be requested from CFF. Indirect costs may be requested for all expenses except for the following:

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

**\*For applications that include a subcontract with a third party, the applicant may request indirect costs only on the first US\$25,000 of each subcontract for the project period.**

- **Budget Justification**

Describe costs listed in the Budget Detail. Use major categories, such as Personnel, Consultant Costs, Equipment, etc. Justify all items and make sure amounts and figures listed in the narrative are consistent with those listed in the Budget Detail(s).

## F. RESEARCH PLAN (template available for download)

- Key figures and legends must be included in the Research Plan and should be of sufficient quality and size to be evaluated by the reviewer. If uploaded as Appendices, they will NOT be reviewed.
  - Type the PI's name in the space available in the header of the document. The template available will track page numbers at the bottom.
  - Page limit: Twelve (12) single-sided pages, not including the Literature Cited, for each project. Applications exceeding this page limit will not be reviewed. Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear and concise manner, while being specific and informative.
- a. **Hypothesis and Specific Aims:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested, if applicable. It is understood that this RFA focuses on technology development and thus may not include a typical hypothesis. The specific aims should be relevant to the mission of the Cystic Fibrosis Foundation. Do not exceed one page.
- b. **Background and Science:** Describe the background. 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 particular those areas listed as areas of special interest to CFF. In addition, describe the relationship of the proposed work to your long-term career goals. Preference will be given to applicants who express an interest in a long-term career in CF-related research.
- c. **Preliminary Results:** If applicable, provide a detailed discussion of any preliminary results. These may be provided in a separate section or incorporated into the experimental design and methods. As new investigators to CF are encouraged to apply, CF-specific preliminary data is not necessary.
- d. **Experimental Design and Methods:** Provide a detailed discussion of the experimental design and methods to be used to accomplish the specific aims. Describe the protocols, including methods for new techniques, and explain potential advantages over existing methodologies. Discuss the data expected to be obtained and the means by which data will be analyzed and interpreted. Discuss potential difficulties and/or limitations of the proposed procedures and alternative approaches to achieve aims. Point out any procedures, situations or materials that may be hazardous to personnel or patients and the precautions to be exercised.
- e. **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 award 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.

- f. **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).

**G. COLLABORATIVE PROGRAM DESCRIPTION (template available for download)**

Collaborative proposals should include a five (5) page maximum overview clearly identifying:

- a. The PI who will assume the overall lead of the program
- b. The overarching aims of the proposal
- c. The goals and importance of each individual project
- d. An explanation of how synergy between projects contributes to the overall aims
- e. A plan for ongoing and regular communication, nature of the collaboration, and sharing of reagents and data as required
- f. Consultant arrangements or outside collaborations are also allowed and should be justified.

**H. LETTER(S) OF SUPPORT FOR COLLABORATIVE INVESTIGATORS (upload as PDF documents)**

Signed Letters of Support and/or Collaboration: A Letter of Collaboration from Co-PIs, if any, should be uploaded and included in the application. Investigators new to CF research are strongly encouraged to consult or collaborate with an established CF investigator/clinician either at their own institution or another. An investigator is considered new to CF if they have not previously (1) published in CF or (2) received extramural funding for a CF-focused research project. A letter of support from the collaborator/consultant should be included with the application, explicitly describing how the proposed work is relevant to CF and how the collaborator/consultant will assist the investigator (such as providing scientific expertise or CF-relevant samples and reagents).

**I. LETTER(S) OF SUPPORT FOR INVESTIGATORS NEW TO CF RESEARCH (upload as PDFs, if applicable)**

**Note:** *\*Not required for experienced CF investigators, e.g. recipients of CFF/past CFFT funding, investigators with recent publications in the field.*

Investigators new to CF research are strongly encouraged to consult or collaborate with an established CF investigator/clinician either at their own institution or another. An investigator is considered new to CF if they have not previously (1) published in CF or (2) received extramural funding for a CF-focused research project. A letter of support from the collaborator/consultant should be included with the application, explicitly describing

how the proposed work is relevant to CF and how the collaborator/consultant will assist the investigator (such as providing scientific expertise or CF-relevant samples and reagents).

**J. VERIFICATION OF APPLICANT INSTITUTION'S TAX STATUS (upload as PDF documents)**

The CFF Grants and Contracts Office must have a copy of the applicant institution's current W-9 and 501(c)3 letter, or other documentation verifying its Federal tax status, and will not issue Award Letters to Awardees if these documents are not received and on file.

- Applicants from for-profit organizations must submit a copy of the applicant institution's W-9 and IRS documentation verifying the organization's Federal tax status. Awards are not issued prior to having these documents on file with the CFF 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. ORGANIZATION ASSURANCES & CERTIFICATIONS (upload under Appendices template type)**

CFF requires, as applicable, that all U.S.-based awardees obtain Institutional Review Board (IRB) approvals for human subject research, Institutional Animal Care and Use Committee (IACUC) approval for animal research, and Institutional Biosafety Committee (IBC) approval for recombinant DNA research (see additional information regarding these approvals below). Copies of these approvals, if available at the time the application is submitted, must be uploaded with the application as appendices. CFF will not release payments to awardee institutions until these documents are received and on file with the CFF Grants and Contracts Office.

Awardees based outside of the U.S. must comply with the applicable equivalent regulations in their respective countries and provide copies of approvals as soon as they are available. CFF will not release payments until these documents are received and on file with the CFF Grants and Contracts Office.

**Research Involving Human Subjects:** CFF policy pertaining to the protection of individuals as research subjects requires that for each proposal awarded, the awardee 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 the Department of Health and Human Services policies found at <https://www.hhs.gov/ohrp/regulations-and-policy/index.html>. In the event the IRB has determined a study is exempt, documentation demonstrating the exempt status must also be submitted to the CFF Grants and Contracts Office.

**Research Involving Recombinant or Synthetic Nucleic Acid Molecules:** All research involving recombinant or synthetic nucleic acid and human gene transfer studies supported by CFF must meet the requirements contained in the document NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (updated April 2016). This publication and announcements of modifications and changes to the NIH Guidelines are available from the Office of Science and Policy, National Institutes of Health, 6705 Rockledge Drive, Ste 750, MSC 7985, Bethesda, MD, 20892-7985 or online at <http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines>.

**Research Involving Animals:** Applications submitted to CFF involving the use of animals must meet the guidelines of the National Institutes of Health found at <https://grants.nih.gov/grants/olaw/olaw.htm>, which require that all proposed studies be reviewed and approved by an Institutional Animal Care and Use Committee (IACUC). In addition, CFF awardee 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.

**L. INTERNATIONAL INSTITUTION FORM (template available for download, if applicable)**

Applicants whose institution is not a United States based-entity must complete the International Institution Form. **Upload a PDF version of the completed and signed form, together with the following documents\*:**

- A copy of the institution's most recent Mission Statement.
- A copy of the institution's tax status documentation or equivalent, or a letter stating it is not available.
- A brief description of other sources of support, such as official awards, private endowments, and commercial activities, received by the institution.
- A copy of the institution's Standard Operating Procedure(s) or relevant policy to ensure that funds provided are neither distributed to terrorists or their support networks, nor are funds used for activities that support terrorism or terrorist organizations.
- For-profit institutions must submit a complete list of key employees, members of the governing board, and/or other senior management.

Applicants who have provided these documents within the past three (3) years are not required to resubmit them. However, if any of the above documents have been updated since they were previously submitted, please upload any updated documents. The CFF Grants and Contracts Office will contact applicants if documents are outdated or missing.

**\*Applicants must provide English translations for all non-English documents, including material provided in support of the Research Plan.**

**M. APPENDICES (upload materials as PDF documents, if applicable)**

Appendices are restricted to the following two (2) categories:

- Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable.
- Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal may be uploaded in PDF format.

**10. PI Data Sheet:** Fill in the required fields, save and exit.

**11. Validate:** Upon completing the application, click on the “**Validate**” button on the main screen. Attend to any omissions/errors as prompted onscreen, and then click “**Validate**” again.

**12. Print Face Pages:** Follow the prompts on the screen to generate and print a Face Page. The Face Page will be populated automatically with data entered in the online application (applicant's name, institution, title of application, etc.). The Face Page must be signed by the Principal Investigator and Authorized Institutional Official and uploaded in Section #9. Co-Principal Investigators, if any, are not expected to sign the Face Page. **Note: CFF will not submit applications for committee review if it does not have the Face Page on file signed by the Principal Investigator and Authorized Institutional Official.**

**13. Submit:** Click on the blue button with white lettering.  CFF will not receive your application unless the “**Submit**” button is clicked.

**Confirmation:** Applicants will receive an e-mail confirmation from proposalCENTRAL (not from CFF) that the Application was successfully submitted. This e-mail will be your only acknowledgement. If you do not receive this confirmation, please contact proposalCENTRAL immediately to ensure that your submission was submitted and processed.

**For technical support with the online application:**

proposalCENTRAL at [pcsupport@altum.com](mailto:pcsupport@altum.com) or  
800-875-2562 on weekdays, 8:00 a.m. to 5:00 p.m. (Eastern)

**For program/content information:**

CFF Grants and Contracts at [grants@cff.org](mailto:grants@cff.org) or 301-841-2614

## VIII. ELECTRONIC APPLICATION CHECKLIST

**Application Deadline: Tuesday, March 12, 2019 at 5:00 PM (ET)**

Submit online through proposalCENTRAL: <https://proposalcentral.altum.com/>

### Face Page which includes:

- Signatures
  - Principal Investigator (Co-PI's are not required to sign)
  - The Official authorized to sign on behalf of the Awardee Institution
- Applicant/PI information (online)
- Complete Institution and PI Contact Information, including correct mailing address (online)
- Organization Assurances (check those that apply online/complete the required information)
  - Human Subjects Certification
  - Recombinant DNA/Biosafety Information
  - Research Involving Animals information

### Research Plan, Supporting Documents and Appendices:

- Abstracts ~ Summary of Relevance ~ Responsiveness - (complete online)
- Biographical Sketches for Key Personnel - (upload)
- Results of Past and Current CFF/CFRT Support - (upload)
- Other Support (NIH Format) - (upload)
- Facilities Available - (upload)
- Budget Detail for each year - (upload)
- Budget Justification for each year - (upload)
- Research Plan - (upload)
  - Hypothesis and Specific Aims
  - Background and Significance
  - Preliminary Results
  - Experimental Design and Methods
  - Consultants/Collaborative Arrangements
  - Literature Cited (not included in Research Plan page limitation)
- Collaborative Program description – (upload)
- Letter(s) of Support for Collaborative Investigators – (upload as PDFs)
- Letter(s) of Support for Investigators New to CF Research – (upload as PDFs)
- Verification of Applicant Institution's Tax Status - (upload)
  - W-9 (U.S. applicants) or W-8BEN-E (non-U.S. applicants)
  - Federal (IRS) tax status letter (U.S.-based applicants) or equivalent tax status letter, or letter indicating it is not available (non-U.S.-based applicants)
- International Institution Form (non-U.S.-based entities only - upload, if applicable)
  - Institution's most recent Mission Statement
  - Applicant institution's tax status documentation or equivalent, or a letter stating it is not available
  - Description of other sources of support, such as official awards, private endowments, and commercial activities, received by institution

- Institution'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 institutions must submit a complete list of key employees, members of the governing board, and/or other senior management
- Appendices (upload as PDFs, if applicable)
  - Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable
  - Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal