



Program Name: Therapeutics Development Award with Letter of Intent (LOI)

Brief Program Overview/Description: In an effort to stimulate development of new pharmaceutical products for CF patients, CFF developed the "Therapeutics Development Award" Program. The purpose of this program is to provide funds to companies that will develop commercial products to benefit individuals with CF. Structured as a matching award program, funds will be awarded only if they are matched by the recipient.

Funding Amount: This is generally a two-part program, and funding is determined by which phase the project will pursue. Component (Phase) I – Discovery and/or Preclinical Development and/or Component (Phase) II – Clinical. Funding for Component I is for up to US\$600,000 over no more than a three (3) year period while Component II is in the range of US\$3,000,000 to US\$5,000,000 over no more than a three (3) year period. Additional details are provided below in Section III.

Eligibility:

- Both U.S.-based and non-U.S. based (i.e. international) companies engaged in research and development are welcome to apply.
- Awards will be made for either discovery (against certain CF airway pathogens) or preclinical and initial clinical development activities (all therapeutic areas relevant to CF).
- CFF support may not be used for API manufacture or other chemistry, manufacturing and controls activities, clinical trials involving healthy human subjects, support of senior company personnel engaged in administrative roles or Phase III multi-center clinical trials. These activities may be used as matching funds.

Key Dates:

Published	February 10, 2020 (updated September 10, 2020)
LOI Submission Deadline	Rolling through October 31, 2020
LOI Applicant Notified	Ad-hoc basis
Full Application Deadline	Rolling through October 31, 2020
Committee Review Date	Ad-hoc basis
Notification to Applicants	Ad-hoc basis
Project Start Date	Ad-hoc basis

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I. About the Cystic Fibrosis Foundation

The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.

II. Program and Award Overview

In an effort to stimulate development of new pharmaceutical products for the benefit of persons with CF, CFF developed the "Therapeutics Development Award" Program. The purpose of this program is to provide funds to companies for the development of commercial products to benefit individuals with CF. Structured as a matching award program, funds will be awarded only if they are matched by the recipient.

With pressure on biotechnology companies to assure a return on investment to their shareholders, funds to initiate new exploratory research projects are limited. Funding currently available to companies is typically committed to products in the late stage of development. There has been a recent explosion in knowledge about CF; and a goal of the TDA award program is to provide funds that will spur companies to explore the feasibility of new therapeutic approaches to CF care.

The widespread scope of this program is meant to assure new product candidates are adequately explored. This funding mechanism is intended to support activities ranging from focused discovery efforts, pre-clinical testing and clinical examination of a potential product's initial safety and efficacy. Once safety and proof of concept is demonstrated, CFF expects TDA awardees to obtain other financial support necessary to conduct pivotal Phase III clinical trials necessary for regulatory approval.

Two-Part Program

CFF requires that investigators who seek support through TDA applications submit a Letter of Intent (LOI) in advance of a full funding application. Applicants may be able to by-pass the LOI with prior approval from the CFF Grants and Contracts Office.

The CFF also sponsors a second funding mechanism, Path to a Cure, the Foundation's ambitious research program to support development of treatments for the underlying cause of the disease and, ultimately, a cure for every person with CF.

Industry programs supported through the Path to a Cure will focus on two core strategies to address the underlying cause of CF:

- Restoring CFTR protein when none exists, including for people with CF who have nonsense mutations
- Fixing or replacing the underlying genetic mutation to address the root cause of CF through gene replacement/transfer, gene editing approaches, or stem cell therapy

The Foundation intends to allocate \$500 million through 2025 for these efforts and is challenging potential collaborators to submit proposals that will accelerate the pace of progress for CF drug discovery and development in areas. [Click here for additional information on The Path to a Cure.](#)

III. Funding Amount

Applicants may apply for funding based on the phase of the proposed research, as follows:

Component I – Discovery and/or Preclinical Development Phase: The objective of this phase may be to either apply platform technology to the discovery of compounds which have the potential to be developed into candidate drugs for the treatment of CF airway pathogens or establish the technical merit and feasibility of a new therapeutic intervention. For discovery efforts, qualifying activities include assay development, screening, secondary assay analysis, medicinal chemistry and preliminary compound testing for pharmacokinetics and bioavailability, as well as specificity and determination of mechanism of action.

When a lead compound has already been identified, funding may be used for animal studies, toxicology, pharmacokinetics, and studies determining a potential new agent's delivery. Funding is for up to US\$600,000 over no more than a three (3) year period.

Component II – Clinical Phase: The objective of this phase is to provide support for the continuation of pre-clinical studies and clinical assessment of new interventions, including safety and dose determination studies in CF patients. Funding will not be provided for chemistry manufacturing and controls (CMC) related activities or studies in healthy human subjects. Funding may be in the range of US\$3,000,000 to US\$5,000,000 over no more than a three (3) year period.

Funding Approach

While not required, CFF expects these TDA funding components will be applied for and funded sequentially. An application for Component I will examine the scientific potential of new products whereas applications for Component II studies will involve support for the continuation of Component I developments and patient clinical studies.

Payments are milestone-dependent and will be issued after CFF approval of accomplishment of each milestone (with third party supporting documentation as needed).

IV. Eligibility

- Both U.S.-based and non-U.S. based (i.e. international) companies engaged in research and development are welcome to apply.
- Awards will be made for either discovery (against certain CF pathogens) or preclinical and initial clinical development activities (all therapeutic areas relevant to CF).
- CFF support may not be used for API manufacture or other chemistry, manufacturing and controls activities, clinical trials involving healthy human subjects, support of senior company personnel engaged in administrative roles or Phase III multi-center clinical trials. These activities may be used as matching funds.
- All projects must be conducted in consultation with a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, other funded mechanism by the CFF, or other funding agencies, and subject to approval by CFF.
- Approved awards will be subject to monitoring by a Project Advisory Group (PAG), whose membership is approved by CFF. If applicable, the PAG will determine overall performance of the project. If applicable, the PAG will report, in writing, to CFF on a periodic basis not less than once every three (3) months. Continued support is also dependent on the PAG's approval of project milestones.
- **Milestones:** Each application must contain milestones that are objective achievements demonstrating forward progress for the therapeutic approach and the appropriate timetable for completion of each. Continued funding for the project will be, in part, based upon milestone attainment.
- **Payback:** If a TDA leads to the marketing of a new intervention, CFF will receive reimbursement for its support. Terms will be negotiated prior to finalizing the award, and will typically include reimbursement, plus a multiple following successful regulatory marketing approval, and/or a percentage of net sales. CFF may also require certain rights to take the product forward in the event that the awardee elects not to advance the product.

V. Mentorship Requirements

Not applicable to this RFA

VI. Goals of Research Currently of Interest to CFF/Priority Areas

Areas of Encouragement

Extensive survey input from the CF community (people with CF, family members, caregivers and key opinion leaders) have identified key research Areas of Encouragement that are most important to them. The areas selected by the CF community are listed below in order of prioritization. Applications may address any topic area advancing CF care, treatment, or research. However, applications addressing the following areas are particularly encouraged:

1. Respiratory microorganism Treatment
2. Inflammation
3. Mucociliary clearance
4. Gastrointestinal symptoms (including, but not limited to, GERD, DIOS, and pancreatitis)
5. CF-related Diabetes
6. CF-related Liver Disease (including cirrhosis and non-cirrhosis, gall stones, hepatic steatosis, and other clinical manifestations of portal hypertension)
7. Diet and Nutrition

VII. Review and Award

Applications will be evaluated based on the following:

- The soundness and technical merit of the proposed approach
- The qualifications of the Principal Investigator (PI), supporting staff and CF collaborators
- The relative importance of the proposed intervention to CF care
- The potential of the proposed research for commercial application
- The appropriateness of the budget requested
- The adequacy and suitability of the facilities and research environment
- The adequacy of milestones to assess overall performance of the project

CFF will notify applicants once a funding decision has been made [with a goal of within four (4) months after receiving a full funding application]. **Applications received in October or later are unlikely to obtain approval within the same calendar year.** All successful awardees will be required to execute an agreement specifying the Terms & Conditions of an award before funds are made available.

VIII. Submission Information

A Letter of Intent (LOI) must be submitted and approved prior to submitting a Full Application

Submit online through proposalCENTRAL: <https://proposalcentral.com/>
(Refer to Section IX 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.

General Timeline:

LOI Submission Deadline	Rolling through October 31, 2020
LOI Applicant Notified	Ad-hoc basis
Full Application Deadline	Rolling through October 31, 2020
Committee Review Date	Ad-hoc basis
Notification to Applicants	Ad-hoc basis
Project Start Date	Ad-hoc basis

IX. Letter of Intent Guidelines

LOI Submission Deadline: Rolling through October 31, 2020 by 5:00 PM (EST)

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

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

Documents should be typed using:

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

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

First-time applicants must register to create a username 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.

Once logged in, the award opportunities, including this Request for Applications (RFA), will be listed on the opening screen.

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 “Therapeutics Development Award w/LOI (Rolling Deadline)” 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 next to the in-progress application.

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 complete the additional listed questions.
- 2. Download Templates & Instructions:** Download the available templates applicable to the project, fill them out and upload them when completed in Section #8. Templates available include:
 - Biographical Sketch(es) of Key Personnel
 - Opportunity Summary 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 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 information in the required fields and click “Save”.
5. **Institution:** If a profile was completed upon registration, the applicant’s/PI’s 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:** 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.
7. **Budget Summary:** Fill in the start date and end date and applicable amounts for each year of support requested by completing the online fields (Period 1, 2, 3). Applications for Component I (Discovery and/or Preclinical Development Phase) cannot exceed US\$600,000 over a three (3) year period (direct costs only); applications for Component II (Clinical Phase) may request between US\$3,000,000 to \$5,000,000 over no more than a three (3) year period (direct costs only). All Therapeutics Development Awards are awarded for a maximum of three (3) years. **Note: Matching funds are required and should be indicated in the Total Costs of the Project.** CFF will not provide funds for travel of employees of applicant institution; however, travel of key personnel to CF-related scientific meetings can be considered as matching funds.
8. **Attachments:** Complete the templates downloaded from Section #2 and upload them here as PDF documents. Fill out the fields describing the attachment, select the attachment type from the pull-down menu, enter a description for the attachment in the corresponding field, choose the file to be uploaded, and click the “Upload Attachment” button to upload the file. Do this for each attachment.
 - A. **Biographical Sketch(es) of Key Personnel (NIH 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. **Opportunity Summary Form (template available for download)**
Complete the brief summary of your potential CF opportunity using the provided template on proposalCENTRAL. There is a five-page limit to your summary; please do not exceed the limit.
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. **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 LOI was successfully submitted. This e-mail will be your only acknowledgement. If you do not receive this confirmation, please contact proposalCENTRAL immediately to ensure the application was submitted.

X. Full Application Guidelines

Full Application Deadline: Rolling through October 31, 2020 by 5:00 PM (EST)

Applications must be submitted online at proposalCENTRAL: <https://proposalcentral.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 as shown in Section XIII. ELECTRONIC APPLICATION CHECKLIST.

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

Full applications for support of these projects will **only** be accepted if the applicant has an **approved** Letter of Intent (LOI) on file with CFF or has been invited to bypass the LOI stage. Notifications of LOI approval are sent via email from the proposalCENTRAL system. Once an applicant has been notified that the LOI was approved, applicants can access and complete the full application by logging in to proposalCENTRAL and clicking the **“Proposals”** tab, then the **“Edit”** button to the left of the screen. Please follow the directions in this section and on proposalCENTRAL.

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.

Applicants without an approved LOI must first go to proposalCENTRAL at <https://proposalcentral.altum.com/> to initiate an LOI or to receive a bypass based on prior discussion with appropriate CFF Personnel. Applications received without an approved LOI will not be reviewed.

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 complete the additional listed questions.
- 2. Download Templates & Instructions:** Download the templates applicable to the project, fill them out and upload them in Section #9. Templates available include:
 - Research Plan
 - Budget Detail
 - Budget Justification
 - Biographical Sketch(es) of Key Personnel
 - Data Safety Monitoring Plan (if applicable)
 - Facilities Available
 - International Institution Form (if applicable)
- 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 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. Click on “Accept Changes”.

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:** In the space provided online for abstracts, provide a statement of no more than 250 words (up to 2,000 characters max, 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:** Provide a statement of no more than 250 words (up to 2,000 characters max, including spaces) summarizing the relevance of the proposed research to the health and well-being of CF patients, for a scientific audience who may or may not have a background in the subspecialty of the proposed research. All applications are reviewed and scored not only on scientific merit but also on relevance to CFF’s mission:

The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.
7. **Budget Summary:** Fill in the start date and end date and applicable amounts for each year of support requested by completing the online fields (Period 1, 2, 3). Applications for Component I (Discovery and/or Preclinical Development Phase) cannot exceed US\$600,000 over a three (3) year period (direct costs only); applications for Component II (Clinical Phase) may request between US\$3,000,000 to \$5,000,000 over no more than a three (3) year period (direct costs only). All Therapeutics Development Awards are awarded for a maximum of three (3) years. **Note: Matching funds are required and should be indicated in the Total Costs of the Project.** CFF will not provide funds for travel of employees of applicant institution; however, travel of key personnel to CF-related scientific meetings can be considered as matching funds.
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 letters) and status at the time of submitting the application. Refer to Section 9.G. ORGANIZATION ASSURANCES & CERTIFICATIONS below 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, choose the file to be uploaded, and click the “Upload Attachment” button to upload the file. Do this for each attachment.

Below are instructions specific to each template as well as additional information regarding other application components.

A. Research Plan (template available for download)

- Page limit: thirty (30) single-sided pages, including the Literature Cited. Applications exceeding this page limit will not be reviewed.
- At the top of each page, in the header, type the PI's name. The available template will track page numbers at the bottom.
- Each Component (if applicable) must be clearly identified within the Research Plan.
- Applications with a Clinical Phase must include a Data Safety Monitoring Plan (DSMP). See Section 9.D below for details.

Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear, concise manner, while being specific and informative.

- Hypothesis, Specific Aims and Milestones Outline:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. Milestones must be outlined and a timetable for the completion, based upon the requested period of support, must be provided.
- Significance:** Briefly describe the background of the present proposal. Critically evaluate existing knowledge and specifically identify the gaps which the project is intended to fill. Specifically, discuss the unmet need the therapeutic intends to fill and its projected impact on CF patient survival, pulmonary exacerbations (duration and/or frequency and CF patient quality of life in the context of existing and emerging CF therapies). 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 the development of new therapies for CF patients.
- Experimental Design, Methods and Milestones:** Describe the protocols, including methods for new techniques, and explain potential advantages over existing methodologies as they apply to each milestone attained. Discuss the data expected to be obtained and the means by which data will be analyzed and interpreted. If clinical studies are involved, provide details of the methods for patient selection and care. 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. Applications will be reviewed and evaluated based upon the experimental design and methods used to achieve the milestones outlined above (item a). All applications will be reviewed based upon the appropriateness of the milestones, the timetable for the completion of milestones, and the approaches outlined to achieve milestones to achieve the development of new therapies for CF patients.
- 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). In addition to letters of collaboration, curricula vitae must also be provided. If clinical material required by this award is to be furnished by other individuals, include a statement from these individuals agreeing to their participation. All applications must include the name, biosketch, and a letter of support from a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, or other funded mechanism by the CFF.
- 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).

B. Budget Detail and Budget Justification (separate templates available for download)

Fill out the Budget Detail and Budget Justification templates **for all years of support requested**. In the space provided on each page, indicate the year or period as well as start and end dates for the proposed budget period. Separate Budget Details are required for Component I (up to **US\$600,000** over three (3) years) and Component II (between US\$3,000,000 to US\$5,000,000 over three (3) years). The budgets for both Component I and Component II must include a plan that utilizes both CFF and applicant funds. **The CFF dollars must be matched at least one-to-one**; however, greater contributions of company funds are acceptable. *Note: CFF support cannot be dedicated to either CMC-related activities or clinical trial costs that involve healthy human subjects.* TDA awards do not provide funds for travel; however, travel of key personnel to CF-related scientific meetings may be considered as matching funds. *Be sure the Budget Detail matches the online budget summary in Section #7.*

Budget Detail – Direct Costs

Salary & Benefits - 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. **Total FTE costs may not exceed US\$200,000 per person per year.** 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 patient research costs 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.

Subcontractors – Detailed budgets for each subcontract, including indirect costs, must be provided for each year of support (complete and upload a Budget Detail and Budget Justification template for each subcontract). Negotiations of subcontracts are between the applicant institution and the subcontractor.

Major Equipment - List all items of equipment greater than \$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.

Patient Research Costs – Funds may be requested for patient research costs specifically related to the proposed research and not considered routine care. The basis for estimating funds requested in this category should be justified and applicants must provide detailed information regarding the proposed costs (e.g., number of procedures, cost per procedure, ancillary costs). The scientific need for patient research costs will be considered in the review. Negotiation of these costs are between the applicant institution and the service provider.

If approved as part of the application, patient research costs are capped at the amount requested in the budget and under no circumstances is CFF or CFF responsible for any costs that are later determined non-covered by third party insurers. Applicants and applicant institutions acknowledge that CFF is solely a provider of funding for the research performed under an approved award and not a sponsor of the research as defined by the FDA (21 CFR §312.3(b)).

Consumable Supplies – Itemize supplies e.g. disposables, reagents, 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.

Other Expenses - Itemize other expenses by major categories such as duplication costs, publication costs, Data Safety Monitoring Plan (DSMP) related-expenses (if applicable), computer charges, equipment maintenance, etc. Justify all items.

Budget Detail – Indirect Costs

Indirect costs are not allowable.

Budget Justification

Describe costs listed in the Budget Detail. Use major categories, such as Salary & Benefits, Consultant Costs, Major 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).

C. 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.

D. Data Safety Monitoring Plan (template available for download, complete if applicable)

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. Large, multi-center CFF-funded interventional clinical trials may be required to utilize a Data Safety and Monitoring Board (DSMB). In addition, because its members are CF clinicians and clinical trial experts, CFF strongly encourages and may require that investigators utilize the CFF DSMB for any other interventional CF clinical trial that meets one or more of the following criteria:

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

Note: *On the available template, please check whether a DSMP is required and upload the template regardless of the response.*

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
 - Involves the use of a new chemical or drug for which there is little or no toxicology data in humans
 - A gene therapy study or research involving recombinant DNA or RNA molecules (gene transfer)
 - 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 stopping rules for the study subjects or for the overall 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 the CFF DSMB, provide the frequency of meetings, the reporting requirements, including AEs and SAEs, and the procedure for interim reporting as necessary. If this information is not available at the time of submission of the application, note that CFF will not release awarded payments until it is provided.

Registrations for Investigator-Initiated Clinical Trials:

- [Clinicaltrials.gov \(United States\)](https://clinicaltrials.gov): Applicants are required to register all non-exempt human subject studies in the ClinicalTrials.gov database to ensure information is freely available on CFF-funded trials within the community. The registration should be no later than twenty-one (21) days after the first subject is enrolled. CFF requires copies of documentation confirming this registration, when applicable.
- [EudraCT Registration \(European Union\)](https://eudra-ct.europa.eu): For interventional clinical trials with medicinal products conducted in the European Union, the Institution must provide documentation to CFF confirming registration of the clinical trial when applicable.

E. 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.

F. Verification of Applicant'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.

G. Organization Assurances & Certifications (upload as Appendices, if applicable)

Research Involving Human Subjects: CFF policy pertaining to the protection of individuals as research subjects requires that for each proposal awarded, 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 found at <https://www.hhs.gov/ohrp/regulations-and-policy/index.html>. IRB status must be indicated on the "Organization Assurances" section of the application in proposalCENTRAL. CFF will not release awarded funds until this certification of IRB approval is received and on file with the Grants and Contracts Office. This certification of IRB approval, if available at the time of application, should be included as an appendix to the application. For interventional and observational studies involving human subjects, the IRB submission date must occur within 30 days following award notification.

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 2019)*. 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 <https://osp.od.nih.gov/biotechnology/nih-guidelines/>

The purpose of the *NIH Guidelines* is to specify practices for the construction and handling of: (i) recombinant nucleic acid molecules; (ii) synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, or (iii) cells, organisms, and viruses containing such molecules.

CFF policy pertaining to recombinant and synthetic nucleic acid research requires that the applicant institution certify in writing that an IBC has reviewed and approved the procedures involving recombinant and synthetic nucleic acids in accordance with the *NIH Guidelines*. IBC status must be indicated on the "Organization Assurances" section of the application in proposalCENTRAL. CFF will not release awarded funds until this certification of IBC approval is received and on file with the Grants and Contracts Office. This certification of IBC approval, if available at the time of application, should be included as an appendix to the application.

Research Involving Animals: Award 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. IACUC status must be indicated on the “Organization Assurances” section of the application in proposalCENTRAL. CFF will not release awarded funds until this certification of IACUC approval is received and on file with the Grants and Contracts Office. This certification of IACUC approval, if available at the time of application, should be included as an appendix to the application.

H. International Institution Form (template available for download, if applicable)

Applicants whose awardee 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 Exemption Letter or equivalent, if institution is a nonprofit.
- 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. If your institution does not have a relevant policy, please provide a statement signed by an institutional official indicating that award funds will not be used to 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 must provide English translations for all non-English documents, including material provided in support of the Research Plan.**

I. Appendices

- Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable
- Up to four (4) reprints of the applicant’s work relating to the general area of research in the proposal
- Letters of reference, support, and/or collaboration, including a letter of support from a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, or other funded mechanism by CFF
- Other materials pertinent to the proposal, not already described. Please upload only the most relevant documents, as excessive materials may not be reviewed

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

11. 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 #7. Co-Principal Investigators, if any, are not expected to sign the Face Page.

12. 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.

13. Submit: Click on the gray button with blue 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.

XI. Other Information

Not applicable to this RFA

XII. Contact Information

For technical support with the online application:

proposalCENTRAL at 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 or 301-841-2614

XIII. Electronic Application Checklist

LOI Submission Deadline: Rolling through October 31, 2020 by 5:00 PM (EST)

Full Application Deadline: Rolling through October 31, 2020 by 5:00 PM (EST)

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

LETTER OF INTENT

- Biographical Sketch(es) of Key Personnel (upload)
- Opportunity Summary Form (upload)

FULL APPLICATION

Face Page (upload) which includes:

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

Research Plan & Supporting Documents

- Scientific and Lay Abstracts, Relevance Statement (complete online)
- Research Plan (upload)
 - Hypothesis, Specific Aims and Milestones Outline
 - Significance
 - Experimental Design, Methods and Milestones
 - Consultant Arrangements
 - Literature Cited
- Budget Detail individually for each year requested (upload)
- Budget Justification individually for each year requested (upload)
- Biographical Sketch(es) of Key Personnel (upload)
- Data Safety Monitoring Plan (for applications with a Clinical Phase download template and upload as PDF document)
- Facilities Available (download template, upload as PDF document)
- International Institution Form (if applicable, download template and upload as PDF documents)
 - Institution's most recent Mission Statement
 - Institution's tax status documentation 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 institution must submit a complete list of key employees, members of the governing board, and/or other senior management
- Verification of the Applicant Institution's Tax Status (upload)
 - W-9 (US applicants) or W-8BEN-E (non-US applicants)
 - 501(c)3, IRS Form 147C or equivalent tax status letter
- Appendices (upload as PDF documents, if applicable)
 - Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable

- Up to four (4) reprints of the applicant's work relating to the general area of research in the proposal, if applicable
- Letters of reference, support, and/or collaboration, including letter from a CF-identified investigator representing a CFF-accredited Center, CF-supported Therapeutic Development Center, or other funded mechanism by the CFF
- Other materials pertinent to the proposal, not already described. Please upload only the most relevant documents, as excessive materials may not be reviewed.