



**Program Name:** Path to a Cure (PTAC): Industry Award with LOI

**Brief Program Overview/Description:** The *Path to a Cure* is the Foundation's research program to support development of treatments for the underlying cause of the disease and, ultimately, a cure for every person with CF. The Foundation has made an initial commitment of \$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.

**Funding Amount:** The level of awards given through the *Path to a Cure* Initiative are expected to be substantially higher than those through the regular CFF Therapeutic Development Award (TDA) program, potentially up to tens of millions of dollars. Contract terms are negotiated prior to finalization of the agreement.

**Eligibility:**

- Both U.S.-based and non-U.S. based (i.e. international) companies engaged in research and development are welcome to apply.
- Awards may be made for either discovery, platform development for gene delivery and editing strategies, preclinical and/or clinical development activities that support development of treatments that address the underlying cause of CF.
- It is recommended that projects be conducted in consultation with CF scientists/investigators knowledgeable in the specific aspects of the project.
- *Additional eligibility requirements can be found in Section IV below.*

**Key Dates:**

Current Version Published	May 13, 2020 (updated September 10, 2020)
LOI Submission	Rolling
LOI Applicant Notified	Generally, within 2 weeks of receipt
Full Application	Rolling
Notification to Applicants	Funding decision goal - 4 months after receipt of full application
Project Start Date	As agreed upon

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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 focused on development of treatments that address the underlying cause of and, ultimately, a cure for every person with CF, the CFF has initiated its Path to a Cure funding mechanism. The Foundation has allocated \$500 million through 2025 for these “Path to a Cure” efforts and is challenging potential collaborators to submit proposals that will accelerate the pace of progress for CF drug discovery and development in described areas. Structured as a matching award program, funds awarded are expected to be matched by the recipient.

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 that from 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.

In addition to funding, the Foundation offers partners a range of resources to de-risk CF drug discovery and development. This includes access to a robust community of leading academic researchers, preclinical CF-related model systems and noncommercial research tools, infrastructure for preclinical development, and the world's largest network of CF clinical trial sites. Additionally, consulting advice on trial design is supported through the [Therapeutics Development Network Coordinating Center](#).

### **Two-Part Application Program**

In order to ensure a proposed program is consistent with our goals and needs, Companies and/or investigators who seek support through the Path to a Cure initiative should contact the CF Foundation to discuss the research program and its applicability to the program. This may be followed by submission of a Letter of Intent (LOI) in advance of a full funding application. In rare occasions when a program has already been extensively discussed with the CFF, applicants may be able to by-pass the LOI with prior approval from the CFF Grants and Contracts Office.

## **III. Funding Amounts**

The level of awards given through the Path to a Cure initiative will vary depending on a specific proposal but the PTAC program expects some awards to be substantially higher than those made for standard CFF industry TDAs; up to tens of millions of dollars. The structure of CFF's investment in the program is also flexible and may include milestone-based payouts similar to the TDA program, equity investment, or other strategies beneficial to both parties. Contract terms are negotiated prior to finalization of the agreement.

## **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 may be made for either discovery, platform development for gene delivery and editing strategies, and preclinical and/or clinical development activities that support development of treatments that address the underlying cause of CF.
- It is recommended that projects be conducted in consultation with CF scientists/investigators knowledgeable in the specific aspects of the project.
- 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 determined at the time of contract

negotiation. Milestone completion and subsequent funding, if applicable, may be dependent on the PAG's review and approval.

### **Financial Return to CFF**

If a Path to a Cure award leads to the development of a new therapy, drug, product or technology that is marketed or meets certain other specified milestones, CFF may receive a financial return for its award. The specific terms of any such financial return will be negotiated and agreed upon prior to finalizing the award and are generally dependent on factors such as the stage(s) of development that is(are) funded, and the magnitude of the award.

## **V. Mentorship Requirements**

*Not applicable to this RFA*

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

**Path to a Cure Research Areas of Interest and Priority areas include but are not necessarily limited to the following:**

- Preclinical
  - Identify viable readthrough compounds and other strategies to support development of treatments for people with nonsense mutations.
  - Platform development for gene delivery and editing strategies
- Targets
  - Develop methods to target appropriate cell(s) in the lung, GI tract, and other tissues affected by CF that can be used for CF genetic-based therapies.
- Delivery
  - Develop vectors that efficiently target and deliver nucleic acid cargo to the correct cells in the correct tissue without inducing an immune response (allowing for re-administration).
- Editing
  - Develop effective gene editing methods, amenable to clinical development, to correct mutations in the CFTR gene.
- Clinical Studies
  - Advance treatments to the clinic with a high potential to benefit people with CFTR nonsense and rare mutations that are not correctable by CFTR modulators.

Any commercial programs developing therapies or therapeutic platforms with the potential to advance these goals will be seriously considered. The amounts of awards provided through the *Path to a Cure* Initiative are expected to be substantially higher than those through the CFF Therapeutics Development Award (TDA) program (<https://www.cff.org/Research/Researcher-Resources/Awards-and-Grants/Research-Awards/Industry-Funding-Opportunities/>). Contract terms will be negotiated prior to finalization of any agreement.

## **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 Company Leadership, 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.

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
LOI Applicant Notified	Generally within 2 weeks of receipt
Full Application Deadline	Rolling
Committee Review Date	Ad-hoc basis
Notification to Applicants	Funding decision goal of 4 months after receipt of a full application
Project Start Date	As agreed upon

### IX. Letter of Intent Guidelines

**LOI Submission Deadline: Rolling**

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 “**Path to A Cure (PTAC): Industry Award with 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 any additional 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/organization 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 **Note: Matching funds are required and should be indicated in the Total Costs of the Project.**
- 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 pulldown 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**

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.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 any additional 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. **Note: Matching funds are required and should be entered in the “Total Matching Costs” field at the bottom of the page. Please refer to section 9.B. below for examples of acceptable matching fund costs.** In Section #2, you must also have downloaded a Budget Detail template and a Budget Justification template which you will upload, once completed, in Section #9.
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.

- a. **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 outlined.
- b. **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.
- c. **Experimental Design, Methods and Milestones:** 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. 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

desired outcomes/milestones.

- d. **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.
- e. **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. The budgets must include a plan that utilizes both CFF and applicant funds. **The CFF PTAC dollars must be matched at least one-to-one;** however, greater contributions of company funds are acceptable. **Matching funds may include activities such as: Travel of key personnel to CF related scientific meetings; Chemistry Manufacturing and Controls; Costs associated with normal human volunteer trials. 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 \$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, upload 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://eudract.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](mailto:pcsupport@altum.com) or  
800-875-2562 on weekdays, 8:00 a.m. to 5:00 p.m. (Eastern)

**Application inquiries:**

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

**For program/content information:**

Lindsey Beaman at [lbeaman@cff.org](mailto:lbeaman@cff.org) and/or Maria Wang at [mwang@cff.org](mailto:mwang@cff.org)

### XIII. Electronic Application Checklist

**LOI Submission Deadline: Rolling**

**Full Application Deadline: Rolling**

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

#### **LETTER OF INTENT**

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

#### **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 organization
- Applicant/PI information (online)
- Complete Institution and PI Contact information, including correct mailing address (online)

##### **Proposal/Research Plan & Supporting Documents**

- Research Plan (upload)
  - Hypothesis, Specific Aims and Milestones Outline
  - Significance
  - Experimental Design, Methods and Milestones
  - Consultant Arrangements
  - Literature Cited (not included in Research Plan page limitation)
- 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
- Facilities Available
- 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
- International Institution Form (if applicable)
- 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
  - 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