Program Name: CFF/NIH K-Unfunded Award

Brief Program Overview/Description: In an effort to assure that all meritorious CF-focused research and early career investigators are supported, CFF has developed the CFF/NIH K-Unfunded Award mechanism to provide bridge funding. The objective of this Request for Applications (RFA) is to support excellent CF-focused researchers whose projects have been submitted to and approved by the NIH but cannot be supported by available funds. In order to be eligible for this program, applications must fall within 10 points of the applicable review priority score.

Funding Amount: The maximum award amount is $80,000 per year for up to two years (Direct Costs Only); indirect costs are not allowable. Personnel costs may not exceed 50% of total costs. *Note: the level of funding will be determined by CFF following review by the designated medical/scientific advisors.*

Eligibility:
- Candidates must be U.S. citizens or U.S. permanent residents (must have obtained permanent residency prior to the time of application)
- The application must have been reviewed by an NIH study section and presented to an institute council within 12 months of applying for CFF support.
- Applications must have been submitted to NIH as a K01, K08, K22, K23, K24, K25 or K99/R00 application and fall within 10 points of the applicable priority score. If an application has been submitted to NIH multiple times, the most recent submission must have been scored in this range to be considered.
- Additional eligibility requirements are outlined below in Section IV.

Key Dates:

Published:	May 13, 2020
LOI Submission Deadline:	N/A
LOI Applicant Notified:	N/A
Full Application Deadline:	rolling through November 2, 2020
Committee Review Date:	rolling
Notification to Applicants:	12 to 16 weeks post submission
Project Start Date:	As determined by applicant

Table of Contents:

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.

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

II. Program and Award Overview

CFF has developed its research programs to complement work at the National Institutes of Health (NIH). Support from CFF, through various mechanisms, is intended to provide support for the development of sufficient preliminary data to make CF-focused investigators highly competitive in the NIH review process. However, as a result of funding constraints on the NIH, coupled with the growing interest in CF research, occasions arise in which highly meritorious grantees are favorably reviewed by the NIH but not funded. In an effort to assure that all meritorious CF-related research is supported, and to support the career development of CF-focused researchers, the CFF has developed the CFF/NIH K-Unfunded Award mechanism to provide bridge funding for well qualified applicants. The objective of this Request for Applications (RFA) is to support excellent CF-related research projects performed by applicants with an intent to pursue a career in CF-related research that have been submitted to and approved by the NIH but cannot be supported by available funds.

CFF does not intend to assume the role of the NIH or other governmental funding agencies, but instead wishes to ensure that the momentum in CF research and development of a cohort of CF-focused researchers are not irreversibly slowed due to budget constraints. The CFF/NIH K-Unfunded Award offers a temporary mechanism for supporting highly meritorious K-award applicants until NIH funding can be obtained. The CFF will continue to vigorously encourage the NIH to assume support of meritorious CF-focused projects and investigators.

III. Funding Amount

The maximum award amount is $80,000 per year for up to two years (Direct Costs Only); indirect costs are not allowable. Personnel costs may not exceed 50% of total costs. *Note: the level of funding awarded will be determined by CFF following review by the designated medical/scientific advisors.*

IV. Eligibility

- The application must have been reviewed by an NIH study section and presented to an institute council within 12 months of applying for CFF support.
- Applications must have been submitted to NIH as a K01, K08, K22, K23, K24, K25 or K99/R00 and fall within 10 points of the applicable priority score. If an applicant has submitted for another K program and wants to know if it qualifies for this award, please contact the Program Officer, Elizabeth Yu (eyu@cff.org) and grants@cff.org. If an application has been submitted to NIH multiple times, the most recent submission must have been scored within 10 points of the relevant priority score to be considered.
- The original NIH application must be clearly relevant to advancing the CFF mission.
- The investigator should not be receiving other funding for this work. If other funding is obtained at any point (through NIH or other funding bodies) for this work, the CFF award must be relinquished.
- If awarded, a revised application must be submitted to the NIH within one (1) year of receiving the CFF award. Failure to do so will result in the loss of support. Documentation showing resubmission must be provided to CFF as part of the final scientific report.

V. Mentorship Requirements

Not applicable to this RFA

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

Proposed research must be relevant to the CFF's mission and to the health and well-being of people with CF. Applicants are encouraged, but not required, to address an emerging area of potential interest stated below. All applications are reviewed and scored based on the individual, training environment, scientific merit, and relevance to the CFF mission.

Research topics of high priority to the CF Foundation:

- Direct and indirect influences of CFTR modulation on the airway milieu, including resident pathogens, inflammation, mucin structure (tethered and secreted), airway surface liquid (ASL), and mucociliary clearance
- Understanding defects associated with CFTR mutations other than F508del (especially nonsense and other mutations not currently treated by CFTR modulators) and approaches for restoring CFTR function
- Biological mechanisms involved in lung allograft dysfunction/rejection and transplant immunology
- Improved understanding of acquisition, detection, pathogenesis, host-pathogen interactions, and treatment approaches for difficult to treat CF infections (i.e. NTM, MDR Pseudomonas, MRSA, Aspergillus, Achromobacter, Burkholderia, Stenotrophomonas)
- Approaches to understand and treat extra-pulmonary manifestations of CF including (but not limited to):
  - CF related GI issues and the impact of nutritional deficiencies
  - Effects of endocrine system dysfunction in CF, including Cystic Fibrosis Related Diabetes (CFRD)and CF bone disease
  - Mental health

Funding priority will be placed on those projects that will lead to a better understanding of disease mechanisms, pathophysiology, and prevention, and treatment strategies.

VII. Review and Award

Since applications to this program have already been reviewed and scored by an NIH study section, CFF medical/scientific advisors will focus on the following points:

- Commitment of the applicant to pursue a career in CF research
- Training environment and mentoring team to provide high quality training in CF research
- Relevance of the proposed study to issues in CF
- Adequacy of the budget
- Potential for future support by the NIH

All awards are subject to observance of CFF policies and Terms and Conditions in addition to applicable Federal regulations or equivalent regulations in the Awardee Institution's country, based on the type of research involved. All awards and ongoing support are also contingent upon the availability of CFF funds.

Applications may be resubmitted through this mechanism after they have gone through another round of review by NIH, and still have a score within 10 points of the relevant NIH priority score.

VIII. Submission Information

Application Deadline (rolling): through Monday, November 2, 2020 at 5:00 PM (EST)

Submit online through proposalCENTRAL: https://proposalcentral.com/
(Refer to Section X 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:
Application Deadline _____ rolling through November 2, 2020
Review _____ rolling
Notification to Applicants _____ 12 to 16 weeks post submission
Project Start Date _____ As determined by applicant

IX. **Letter of Intent Guidelines**
Not applicable to this RFA

X. **Full Application Guidelines**
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/

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.

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

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

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

Locate the listing for the **"CFF/NIH K-Unfunded Award (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.

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 a project title for the CFF application. Answer the required questions about the title of the NIH unfunded application, the NIH unfunded application number, and in regards to the applicant's prior application and award history with CFF. Also, please indicate if you will be requesting access to the Patient Registry Data or Biorepository Clinical Specimens as outlined in Sections 10 J. and K. respectively.

2. **Download Templates & Instructions**: Download the available templates applicable to the project, fill them out and upload them when completed in Section #10. Templates available include:
   - Application for CFFPR Data and Confidentiality Agreement
   - Budget Detail
   - Budget Justification
   - Response to NIH Summary Statement
   - Revised Research Plan
   - Other Support
   - Facilities Available
   - Data Safety Monitoring Plan

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. **Key Personnel:** In the table online, provide contact information for key personnel included in the application, other than the PI/Applicant. To add a new contact, enter the e-mail address of the person in the available field. Click the "Add contact" icon. Complete the contact form that pops up and click "Save". *Note: if the person is already registered in proposalCENTRAL, some information will be pre-loaded into the contact form.* To edit the person's contact information, click the "Edit" icon in the Actions column to the far right. To delete a person from the table, click the "Delete" icon. *Note: Changes made to the person's contact information will apply to this proposal only. Permanent changes must be made in the person's Professional Profile by the person.*

7. **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.

8. **Budget Summary:** Fill in the start and end date and applicable amounts for the support requested by completing the applicable online fields (Period 1 and/or Period 2). The total budget requested cannot exceed $80,000 per year. Personnel costs may not exceed 50% of total costs.
Note: The Budget Detail and Budget Justification templates downloaded in Section #2 must also be completed for each year of support requested and uploaded in Section #10. The amounts included in this uploaded Budget Detail must match the amounts entered in the Budget Summary online.

9. **Organization Assurances:** Select the type of assurances that are applicable to the project and provide all required information (i.e. IRB, IACUC, and/or IBC/rDNA approval letter and status at the time of submitting the application). Refer to Section N. ORGANIZATION ASSURANCES & CERTIFICATIONS in these guidelines for details.

10. **Revised 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. **Budget Detail and Budget Justification (separate templates available for download)**
    Fill out the Budget Detail and Budget Justification templates for each and all years of support requested. In the space provided on the templates, indicate the year as well as start and end dates for the proposed budget period. (Be sure the amounts entered in the Budget Detail(s) match the amounts in the online budget summary in Section #8).

    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. In accordance with National Institutes of Health (NIH) policy, salary requests may not use an institutional base salary in excess of the current federal salary cap of $197,300; when calculating salary requests, the NIH cap must be adhered to. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all funding agencies and foundations.

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

    Subcontractors – The total cost of each subcontract (directs costs only) should be listed under "Other Expenses" and included in the applicant's direct costs. Separate Budget Details and Justifications must be provided for each subcontract, 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.

Travel – Describe the purpose of any CF-relevant travel. Please note: expenses for travel outside the North American continent for domestic applicants, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable expenses without prior written approval from the CFF Grants and Contracts Office. Travel expenses may not exceed **$1,500 per person, per year**. Additional travel expenses may be requested and will be considered on a case-by-case basis. Registration fees associated with conferences should be listed under "Other Expenses."

Patient Research Costs – Funds may be requested for patient research costs specifically related to the proposed research. The basis for estimating funds requested in this category must 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 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 subcontracts, duplication costs, publication costs, conference registration fees, computer charges, and other research costs (e.g., recruitment flyers, brochures, patient travel cost reimbursement, and reasonable patient stipends for participation), etc. Justify all items. *Note: Tuition costs are not allowable.*

Budget Detail – Indirect Costs
Indirect costs are not allowable.

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

B. **Copy of NIH unfunded application (upload as PDF document)**
A PDF copy of the entire unfunded grant application should be uploaded to proposalCENTRAL (in Section #10) of the online application. When uploading the file:
- Select "Copy of NIH K-Unfunded Application" as Attachment Type from the available drop-down menu.
- Describe attachments as "NIH K-Unfunded Application" in the corresponding field.

C. **Copy of NIH Summary Statement (or equivalent) (upload as PDF document)**
A PDF copy of the entire NIH Summary Statement associated with the unfunded grant application must be uploaded to proposalCENTRAL (in Section #10) of the online application. When uploading the file:
- Select "Copy of NIH Summary Statement" as Attachment type from the available drop-down menu.
- Describe attachment as "NIH Summary Statement" in the corresponding field.

D. **Responses to NIH Summary Statement (template available for download)**
Please provide a point-by-point response to the critiques noted in the NIH Summary Statement and specific plans to address identified weaknesses. There is no page limit to the responses; however, be as concise and succinct as possible.

E. **Revised Research Plan (template available for download)**
- Key figures and legends must be included in the Research Plan and should be of sufficient quality and size to be evaluated by the reviewer(s). If uploaded as Appendices, they will NOT be reviewed.
- Type the PI's name in the space available in the header of the document. The template available will track page numbers at the bottom.
- Page limit: Ten (10) single-sided pages, not including the Literature Cited. Applications exceeding this page limit will not be reviewed. Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear and concise manner, while being specific and informative.

The Revised Research plan should not be a copy of the submitted NIH-unfunded application. Instead, **this section should highlight the scope of work and experiments that will be completed using the funds from CFF if the award is funded**. This section should specifically address weaknesses noted in the NIH Summary Statement as well as the reduced CFF budget. The Revised Research Plan must also include a clear strategy for resubmission of the original application to the NIH. The plan may include the following components:

a. **Hypothesis and Specific Aims:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. The specific aims should be clearly relevant to the mission of the Cystic Fibrosis Foundation. Do not exceed one page.
b. **Background and Significance:** Briefly describe the background. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this research by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF. In addition, describe the relationship of the proposed work to your long-term career goals. Preference will be given to applicants who express an interest in a long-term career in CF-related research.
c. **Preliminary Results:** If applicable, provide a detailed discussion of any preliminary results.
d. **Experimental Design and Methods**: Provide a detailed discussion of the experimental design and procedures to be used to accomplish specific aims. Please discuss: study hypothesis; primary and secondary outcome measures; study sample-inclusion and exclusion criteria; sample size estimates*; subject enrollment including age range; pubertal status (if applicable); sex distribution; randomization scheme (if applicable); description of experimental procedures and schedule including a study time-line; drugs and dosage; measures of compliance; follow-up schedule including a study time-line for full project up to three years; efficacy and safety evaluation, data monitoring and quality control; and a description of your proposed data analysis and statistical procedures for your hypothesis testing. Although no page limit is specified for this section, make every attempt to be concise and succinct.
   *For sample size estimates, please provide all estimates of means, standard deviations, rates or proportions used to calculate each of your sample size or power estimates. Please include in the statistical section whether you will use a one or two-tailed test, the power selected for such a test (if making a sample size calculation), and the reference for your sample size or power calculation. In instances of pilot studies where some of these parameters are unknown, we will accept your best estimates of the unknown parameters if preliminary data are not available, and if your calculation is a preliminary estimate before formal sample size can be

calculated for a larger study. Please identify if you are making estimates from data or from personal estimates. This section must document access to adequate numbers of subjects. If the Sponsor(s) is not a CF Center Director or Co-Director, a letter of support from the Center Director is required (upload as a PDF document in Section #10, as an Appendix).

e. **Limitations and Potential Pitfalls:** 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.

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

g. **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).

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

G. **Letter(s) of Support (upload as PDF documents, if applicable)**
Letters of support should specifically speak to CF priorities and research commitment. Applicants may provide up to two (2) additional letters not already included in the original NIH K Award application. Investigators are strongly encouraged to consult or collaborate with an established CF investigator/clinician either at their own institution or another. A letter of support from the collaborator/consultant should be included with the application (either within the original NIH submission or uploaded here), explicitly describing how the proposed work is relevant to CF and how the collaborator/consultant will assist the investigator (such as providing scientific expertise or CF-relevant samples and reagents). Upload a PDF of the signed letter(s) of support as appendices to proposalCENTRAL (in Section #10).

H. **Letter of Institutional Commitment (upload as PDF document):** A letter of institutional commitment must be provided from the Chair of the applicant's Department at the applicant institution – The letter should clearly describe the institution's commitment to the professional growth and research career of the applicant.

I. **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.

J. **CFF Patient Registry Data Request (if applicable)**
CF Foundation Patient Registry. Applicants whose project will include requesting data from the CF Foundation Patient Registry should check the appropriate box. It is not necessary to check the box for single site studies or studies acquiring Registry data from the biorepository. Please note: the applicant should submit the project for review by the Registry / Comparative Effectiveness Research (CER) committee prior to grant submission. Instruction regarding submission for review are located at: https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/Patient-Registry-Data-Requests/

K. **CFF Biorepository Clinical Specimen Confirmation Letter (if applicable)**
Since 2006, the Cystic Fibrosis Foundation has collected and stored samples from a variety of clinical trials. The CF Foundation has developed a database that combines information from these samples with data from CF clinical trials and the CF Foundation Patient Registry to create a unique and specific sample profile. To request clinical samples to use in the proposed study, download and complete the template from https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/CFFT-Biorepository/. Applicants must supply a letter from the clinical research program manager confirming samples are available for their use with their application. For more information, contact Linh Do, CF Foundation clinical research program manager, at ldo@cff.org or 301-841-2648.

Note: If applicable, funding is contingent upon approval and availability to access clinical specimens.

L. **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): 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): 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.

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

- Applicants from for-profit organizations must submit a copy of the applicant institution's W-9 and IRS documentation verifying the organization's Federal tax status. Awards are not issued prior to having these documents on file with the CFF Grants and Contracts Office.

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

Research Involving Human Subjects: CFF policy pertaining to the protection of individuals as research subjects requires that for each proposal awarded, the awardee institution certify in writing that an Institutional Review Board (IRB) has reviewed and approved the procedures for the use of human subjects, or human organs, tissues and body fluids, in the proposed research, in accordance with the Department of Health and Human Services policies found at https://www.hhs.gov/ohrp/regulations-and-policy/index.html. In the event the IRB has determined a study is exempt, documentation demonstrating the exempt status must also be submitted to the CFF Grants and Contracts Office.

Research Involving Recombinant or Synthetic Nucleic Acid Molecules: All research involving recombinant or synthetic nucleic acid and human gene transfer studies supported by CFF must meet the requirements contained in the document *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (updated April 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/wp-content/uploads/NIH_Guidelines.pdf.

Research Involving Animals: Applications submitted to CFF involving the use of animals must meet the guidelines of the National Institutes of Health found at https://grants.nih.gov/grants/olaw/olaw.htm, which require that all proposed studies be reviewed and approved by an Institutional Animal Care and Use Committee (IACUC). In addition, CFF awardee institutions and laboratories must be accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and/or have other verifiable assurances that the institution and laboratory meet appropriate standards.

O. **APPENDICES (upload materials as PDF documents, if applicable)**
Appendices are restricted to the following four (4) categories:
- Certification of organization assurances (i.e. IRB, IACUC and IBC approvals).
- Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal may be uploaded in PDF format.
- Additional NIH (or equivalent) Biographical Sketches, that are not already included in the original application, should be completed/uploaded for any new key personnel named in the CFF application. *Note: CFF defines "key personnel" as any individual with an advanced degree that will plan an instrumental role in the accomplishment of the research project.*

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

12. **Print Face Pages:** Follow the prompts on the screen to generate and print a Face Page. The Face Page will be populated automatically with data entered in the online application (applicant's name, institution, title of application, etc.). The Face Page must be signed by the Principal Investigator and Authorized Institutional Official and uploaded in Section #10. Co-Principal Investigators, if any, are not expected to sign the Face Page.

13. **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.

14. **Submit:** Click on the gray button with blue lettering. **Submit** 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

Application Deadline (rolling): through Monday, November 2, 2020 at 5:00 PM (EST)

Submit online through proposalCENTRAL: https://proposalcentral.com/

Face Page which includes:
- ☐ Signatures
  - ☐ Applicant
  - ☐ The Official authorized to sign on behalf of the Applicant Institution
- ☐ Applicant information (online)
- ☐ Complete Institution and Applicant Contact Information, including correct mailing address (online)
- ☐ Organization Assurances (check those that apply online/complete the required information)
  - ☐ Human Subjects Certification
  - ☐ Research Involving Recombinant or Synthetic Nucleic Acid Molecules information
  - ☐ Research Involving Animals Information
- ☐ Key Personnel (online)

Research Plan & Supporting Documents:
- ☐ Budget Detail for each year of support requested - (upload)
- ☐ Budget Justification for each year of support requested - (upload)
- ☐ Copy of NIH-Unfunded Application - (upload)
- ☐ Copy of NIH Summary Statement (or equivalent) - (upload)
- ☐ Responses to NIH Summary Statement - (upload)
- ☐ Revised Research Plan - (upload)
  - ☐ Hypothesis and Specific Aims
  - ☐ Background and Significance
  - ☐ Preliminary Results
  - ☐ Experimental Design and Methods
  - ☐ Limitations and Potential Pitfalls
  - ☐ Consultant Arrangements
  - ☐ Literature Cited (not included in Research Plan page limitation)
- ☐ Other Support – (upload)
- ☐ Letter(s) of Support – (upload two (2), if applicable)
- ☐ Letter of Institutional Commitment – (upload)
- ☐ Facilities Available – (upload)
- ☐ Data Safety Monitoring Plan – (upload)
- ☐ Verification of Applicant Institution's Tax Status - (upload)
  - ☐ W-9 (U.S. applicants)
  - ☐ Federal (IRS) tax status letter (U.S.-based applicants) or equivalent tax status letter
- ☐ Appendices (upload as PDF documents, if applicable)
  - ☐ Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if available at the time of application.
  - ☐ Up to three (3) reprints of the applicant's work relating to the general area of research in the proposal
  - ☐ Additional NIH (or equivalent) Biographical Sketches, that are not already included in the original application, should be completed/uploaded for any new key personnel named in the CFF application. *Note: CFF defines "key personnel" as any individual with an advanced degree that will plan an instrumental role in the accomplishment of the research project.*