CYSTIC FIBROSIS FOUNDATION

For application technical support, please contact aminucci@cff.org

Program Name: 2023 Patient Registry Research: Application of Advanced Methods with LOI

Brief Program Overview/Description: The Cystic Fibrosis Foundation (CF Foundation) is requesting Applications (RFA) with a Letter of Intent (LOI) for innovative registry-based analyses that aim to test novel methods to advance the use of the (CFFPR). There are a multitude of use cases for CFFPR data, including research to further knowledge of the natural history of CF, estimate the real-world effect of therapies and quantify CF healthcare utilization. In the era of modulator therapy and future genetic therapies, there is a need for additional research in the utility of novel methods in the analysis of CFFPR data across a broad range of research areas, not limited to the appropriate choice of comparator populations, the impact of selection bias (missing data, loss to follow-up, etc.) on estimation of treatment effects and the impact of reduced frequency of CF care utilization on estimation of population-level summary statistics. This RFA with LOI request will increase our understanding of the strengths and limitations of CFFPR data to help guide the investigator community in the design and implementation of future studies. The CF Foundation is interested in reviewing applications that cover a broad range of methodological approaches, including (but not limited to) causal inference and simulation methods.
Please note: This is a one-time Request for Applications (RFA) with a LOI. Full applications will be solicited by invitation only after review of LOI.

Funding Amount: Applicants may request funding up to $150,000 per year for up to two (2) years, plus an additional twelve (12) percent indirect costs. Additional information can be found in Section III below.

Eligibility Requirements:
- Candidates must be U.S. citizens or U.S. permanent residents (must have obtained permanent residency prior to the time of application).
- Additional eligibility requirements can be found in Section IV below

Key Dates:

Published	June 1, 2023
LOI Submission Deadline	~~July 20, 2023~~ Extended to August 9th, 2023*
LOI Applicant Notified	August 2023
Full Application Deadline	~~October 24, 2023~~ Extended to November 14th, 2023*
Committee Review Date	January 2024
Notification to Applicants	Early February 2024
Earliest Project Start Date	April 1, 2024

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*We highly encourage all applicants to pre-register their profile, institution, contacts, and Title of their application at least two weeks prior to the application deadline. This will help to ensure the CFF Grants & Contracts Management and Administration (GCMA) Team is able to assist all applicants with any potential system-related queries prior to the Application Deadline.

I. About the Cystic Fibrosis Foundation

The mission of the CF Foundation is to cure CF 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 awards are offered to support meritorious research ranging from basic laboratory investigation to clinical management of CF.

CF Foundation Resources

The Cystic Fibrosis Foundation supports the development of a number of helpful tools and resources to assist the research community in accelerating the progress toward new scientific knowledge of and new therapies for cystic fibrosis. For more information on Tools and Resources for the CFF research community, please visit: https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/

CFF Patient Registry Data

The CF Foundation Patient Registry collects information on the health status of people with cystic fibrosis who receive care in CF Foundation-accredited care centers and agree to participate in the Registry. This information is used to create CF care guidelines, assist care teams providing care to individuals with CF, and guide quality improvement initiatives at care centers. Researchers also use the Patient Registry to study CF treatments and outcomes and to design CF clinical trials.

The Cystic Fibrosis Foundation Patient Registry is an invaluable tool for researchers who are interested in conducting studies about people with CF in the United States. About 50,000 individuals have been followed in the Registry, and many have been included for over 20 years. In addition, we recently linked the CF Foundation Patient Registry with the Pediatric Health Information System (PHIS) database. Investigators at PHIS sites can request to use these linked data. Instructions on how to request CFFPR data for your research project is included in the application instructions below.

II. Program Overview

Background:

CF is an autosomal recessive, multisystem disease. Approximately 80% of the 40,000 children and adults in the US affected by the disease participate in the CF Foundation Patient Registry (1). Programs deliver specialized care that emphasizes interdisciplinary collaboration among physicians, nurses, dietitians, social workers, respiratory therapists, pharmacists, and other sub-specialists as needed. Care is managed using clinical practice guidelines, routine pulmonary function testing, monitoring height and weight, and collection of throat cultures or sputum samples and blood draws. Since 1986, data obtained over the course of CF care have been reported annually or quarterly to the CFFPR by CF care teams, with additional encounter-based data available from 2003 to the present.

Context:

The CF Foundation permits secondary analysis of CFFPR data for research questions implemented by established researchers with prior experience in CF research or clinical care. Over 200 research projects have been approved in the past twenty years, with an expanding interest in quantifying the impact of therapies on survival, lung transplantation, lung function, growth and other outcomes. Most analyses propose common statistical methods such as multivariable regression to estimate effects. As new therapies for CF become increasingly dependent on an individual's CFTR variants for eligibility, use of these data become more complex. Choice of appropriate comparator groups, the impact of prior therapies, age of initiation, and changes in data availability over time may entail more sophisticated analytical approaches than previously required.

Goals:
The goal of this RFA with LOI is to identify innovative registry research projects considered relevant to advancing knowledge of CF and to encourage junior investigators (Defined in Section IV below) with expertise in statistics or epidemiology to engage in CF research. Areas of encouragement to address research for specific aspects of CF disease that are of interest are found in Section VI below.

A successful project will use novel methods to address a CF-related research question and demonstrate the utility of a given method for a broad audience of statisticians and clinical researchers. Awardees are expected to publish the results of their research in the peer-review including analytical code or tutorials to enable replication. Awardees must present their research to CFF's Comparative Effectiveness Research Committee before the end of the project.

A limited number of LOIs will be invited to submit full applications. Applications that do not specify how the project can benefit people with CF and advance registry-based research and/or are deemed nonresponsive to areas of interest will not be invited for a full application. Work in this space will inform future grant offerings and is intended to be shared broadly with the CF community.

III. Funding Amounts

- Funding of up to **$150,000 per year for up to two (2) years**, plus an additional twelve percent (12%) indirect costs may be requested.
  - A lead PI must submit one application on behalf of all participating investigators.
  - The budget must include a lead institution with the other participating institution as subcontractors.
- Funding for Year 2 is contingent upon submission and approval of a renewal progress report and the availability of funds.

Direct costs may be requested for:
- Salary and Benefits
- Project supplies
- Computer software/licenses
- Office supplies (i.e., shipping costs and material)
- Travel costs for the North American CF Conference (NACFC)
- Publication costs

Direct costs for the following are unallowable:
- Tuition
- Prospective data collection of any kind in a hospital/clinic setting (no patient recruitment whatsoever)
- Consultant costs: up to 5% FTE can be requested for a CF clinician to serve as a consultant or Co-PI on the project to provide support such as clinical perspective on interpretation of study results, manuscript writing, etc.

Indirect Costs up to twelve (12) percent may be requested from CF Foundation. Indirect costs may be requested for all expenses except for the following:
- Equipment (single items over US$5,000 in value)
- Computer software/licenses

***Applicants may request indirect costs on the first $25,000 of each subcontract per year.**

IV. Eligibility Requirements

- Candidates must be U.S. citizens or U.S. permanent residents (must have obtained permanent residency prior to the time of application).

- Junior investigators are encouraged to apply as the intent of the funding mechanism is to encourage investigators with experience using advanced methods in biostatistics or epidemiology to pursue cystic fibrosis research.
- The lead PI must have prior training in epidemiology or biostatistics, with a focus on secondary analysis of longitudinal observational data and hold an academic faculty or postdoctoral fellowship position. Individuals with a postdoctoral fellowship appointment must have a pending faculty appointment or be otherwise able to demonstrate sufficient support to allow for completion of the project.
- Current recipients of Schwachman, StatNet or other CFF-funded grants intended to support career development may apply in their final year of the award.
- A clinician with experience in CF should be included on the study team. If the lead PI is not a clinician with CF experience or has not previously engaged in CF research, then a CF clinician must be named as either Co-PI or Consultant with at least 5% effort on the project. Industry-sponsored research projects are not eligible to apply through this program and instead should consider applying to the Therapeutics Development Awards program. For additional information, please contact grants@cff.org and copy Elizabeth Cromwell at ecromwell@cff.org.

CFF defines "junior investigator" as any individual who has not received a CFF/CFFT Research Grant or NIH equivalent (e.g. R01, R21, R23) as a Principal Investigator AND is within their first five years of their first academic appointment at the level of Assistant Professor or equivalent. Postdoctoral fellows may also apply.

Applicant is NOT considered a junior investigator if they meet one or more of the below criteria:

- More than five years after their first academic appointment at the level of Assistant Professor (or equivalent)
- Has received a CFF/CFFT Research Grant or NIH equivalent (e.g., RO1, R21, R23)
- Has been promoted to Associate Professor or higher

V. Mentorship Requirements

Not applicable to this RFA

VI. Goals/Projects of Interest/Priority Areas

The objective of this RFA is to support rigorous secondary analysis of CFFPR data with the intent to demonstrate the utility of novel methods in statistics and epidemiology and identify the strengths and limitations of registry data for a given method. Areas of methodological focus may include projects that address these priority areas:

- Novel methods for longitudinal analysis of lung function, height, weight or other outcomes
- Causal inference or other novel methods to estimate treatment effects
- Quantification of bias
- Selection of comparator populations for rare disease studies
- Generalizability
- Methods to account for missing data
- Advances in the analysis of additional data sources linked to registry

The proposed project must demonstrate application of the method(s) to address a research area of importance. The following research areas are of particular interest to the CF Foundation as they will address critical needs of people with CF:

- Respiratory microorganisms (surveillance and treatment)
- Lung function
- Nutrition
- CF-related Diabetes

- CF-related Liver Disease (including cirrhosis and non-cirrhosis, gall stones, hepatic steatosis, and other clinical manifestations of portal hypertension)
- Characterization of CF disease manifestations and management in the era of highly effective modulator therapy
- Utilization of CF care
- Studies that investigate CF disease complications (lung, GI tract, liver, pancreas, endocrine, fertility, etc.)
- Estimation of treatment effects on outcomes such as growth (height, weight, BMI), lung function, survival or transplantation
- Studies that identify and characterize racial, ethnic, and/or societal contributors to CF disease expression and management

Projects designed to test statistical methods with no clinical relevance will not be considered.

VII. Review and Award

Applications will be reviewed and scored by a CF Foundation ad-hoc review committee. Funding of awards is based on the priority score awarded to each application and the recommendations of the review committee. Funding decisions are based on the relevance of the proposed study to the goals of the Foundation, alignment with specific research priorities, and enhancing the existing CF Foundation project portfolio. The goal of the RFA is to expand the breadth of registry-based research and to encourage investigators with experience using advanced methods in biostatistics or epidemiology to contribute to cystic fibrosis research.

All awards are subject to compliance with applicable regulations and CF Foundation policies and are contingent upon the availability of CF Foundation funds.

<u>Applications will be evaluated on the following:</u>

- Relevance to the priority areas stated above
- Methodologic rigor of and rationale for the proposed analyses including clarity of desired outcomes and analytic plans
- Merit, feasibility, and applicability to future CFFPR-based studies as described in the applicant's Project Plan
- PI's background and experience in longitudinal analyses, causal inference, or other novel analytical approaches
- Alignment between proposed budget and research activities

<u>Low priority scores in the reviews commonly result from the following shortcomings of the application:</u>

- Failure to address the evaluation criteria described above
- Incomplete application or documentation
- Inadequate explanation of project design or methods
- Failure to describe potential relevance
- Failure to document the necessary skills or training to accomplish the goals of the proposal
- Failure to identify access to resources outlined in the application
- Insufficient budget justification
- Failure to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the proposed project

CF Foundation may withdraw applications receiving low scores, and/or those deemed nonresponsive to the program announcement before the review committee meeting. In these cases, CF Foundation will notify applicants if their application has been withdrawn without discussion.

Awardees are required to provide CF Foundation with annual progress and financial reports.

VIII. Submission Information

A Letter of Intent (LOI) must be submitted and approved prior to submitting a Full Application. Applicants may only submit one LOI and one full application.

Submit online at https://awards.cff.org
(Refer to Section IX and 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. CF Foundation reviews applications electronically, and only documents submitted online at https://awards.cff.org will be reviewed.

Specific requests regarding a programmatic deviation from these guidelines must be submitted to the Program Officer Elizabeth Cromwell (ecromwell@cff.org) for approval prior to submitting the application. Contact information for technical questions is provided below.

General Timeline:

Published	June 1, 2023
LOI Submission Deadline	~~July 20, 2023~~ extended to August 9th, 2023
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IX. Letter of Intent Guidelines

LOIs Submission Deadline: Wednesday, August 9th, 2023 at 5:00 PM (EDT)

Applications must be submitted online at https://awards.cff.org

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 awards.cff.org, the system will compile them into a single PDF file. You may preview this file by selecting "LOI Application Full Print", as well as exporting the compiled PDF file.*

To login, please visit: https://awards.cff.org

For all first-time applicants in the new Grants Management System, we ask that you pre-register to create a username and password for "http://awards.cff.org" and complete a profile prior to submitting an application. ***Please note:*** Applicants should register their profile using the "Domestic Institution" to ensure

that your profile aligns properly with the institutions where the project will be conducted. We also request that as you begin your application, you enter the title of your project, if available. If you are registered and cannot remember your password, click on the **"Forgot Password?"** link below the **"Login"** fields.

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

Locate the listing for the **"2023 Patient Registry Research: Application of Advanced Methods with LOI"** program. Click on the "Apply" 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 at the bottom of each page *before exiting* in order to save their progress. When you wish to return to your draft application, please do not go through the "Funding Opportunities" tab. Instead, go to the "My Applications" tab in the right corner of the main page. When you are in the "My Applications" tab you will be able to find all your draft applications by clicking on the "Draft Applications" module.

The following sections are displayed as tabs across the application screen. Click on each section and follow the directions. Click "**Save**" as you complete each section.

GENERAL

Enter the title of your project, enter the project start and end dates, select the number of periods being requested, and complete any additional questions. Also, please complete the organizational assurances indications (i.e. IRB approval letter and status at the time of submitting the application) in this section.

CONTACT PROFILE

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, you may update your profile in this section.

Once updated you must "**Save and Validate**" prior to returning to continue your submission.

INSTITUTION

If a profile was completed upon registration, the applicant's/principal investigator's institution will be pre-loaded as the Lead Institution. Domestic applicants must verify their institution by entering the Employer Identification Number (EIN) or Tax Identification Number (TIN) to search the system for the correct institution. **Please be sure to use the dash formatting when entering your EIN/TIN (XX-XXXXXXX).** If the EIN/TIN is not located, you may add the legal institution. Please also confirm if the project site is the same as the legal institution.

<u>Verification of Applicant Institution's Tax Status (upload as PDF documents):</u>
The CFF GCMA 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 GCMA Office.

<u>International Applicants (if applicable):</u>
Not applicable to this RFA

CONTACTS

Please note: The INSTITUTION tab must be completed prior to adding internal contacts to ensure that the contacts are properly associated with the applicant institution.

Complete the required contact fields by searching by name for existing contacts at your institution for each role. If the desired institutional contact is not available in the system, you may select "**Add Internal Contact**" to create a basic contact profile in order to add the individual to your application.

Additional contacts not associated with the applicant institution may also be added. These contacts are considered additional contributors involved in the proposed research plan. These may include consultants, collaborators, or subcontractors. In order to add contacts external to the applicant institution, please select the appropriate "Add Subcontractors" or "Add Consultants/Collaborators" button(s) and add the contacts in the table, then click "Save".
See a How-To Guide Here: https://www.cff.org/sites/default/files/2021-10/GMS-Guide-Applicants.pdf

ABSTRACTS/RELEVANCE

In the space provided online for each abstract, provide a statement of no more than 2,000 characters (including spaces) explaining the subject of the project 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 CF Foundation 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 CF Foundation mission**: All applications are reviewed and scored not only on scientific merit but also on relevance to CF Foundation'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.

  Provide a statement of no more than 3,000 characters (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.

BUDGET

Select the "**Open**" button under the Budget tab and complete the relevant budget categories for each year of funding. Fill in the applicable amounts for each year of support requested by completing the online fields (Periods 1 and 2). All Awards issued through the "2023 Patient Registry Research: Application of Advanced Methods with LOI" program are awarded for up to 2 years at:

- $150,000/year in direct costs (plus an additional 12% indirect costs)

Be sure to click "**Save**" prior to closing the budget window.

LOI UPLOADS

Download the available template applicable to the proposal, upload the completed template in PDF format to the corresponding attachment type within this section. The template available for download is:

- Biographical Sketch(es) of Key Personnel
- LOI Project Description
- CFF Patient Registry Data Request Application (if applicable)

Biographical Sketch(es) of Key Personnel (NIH template available for download)
CFF defines "key project personnel" as any individual with an advanced degree who will play an instrumental role in the research project. An NIH Biographical Sketch form should be completed for each key project personnel and uploaded as PDF. The maximum length for each biosketch is five (5) pages. Personnel must include a biostatistician with a minimum of 5% effort during the entire project period.

LOI Project Description (template available for download)
Upload the completed template in PDF format providing, at a minimum, Title, Introduction, Methods, and Anticipated Impact of Results **(maximum of three (3) pages not including the literature cited).**

Components should include:

- Descriptive title of the proposed project
- Introduction (nature of the problem, current knowledge/studies, rationale used to develop intervention/theory of change, specific aims of the project)
- Methods (Description of context (clinic, patient/family population), intervention(s), approach used to assess impact of process change and/or outcomes, measurement plan, plan for analysis and integration of data from multiple sites, and ethical considerations)
- Anticipated results, measures/outcomes of interest
- Discussion of anticipated limitations, broad applicability, sustainability, spread and scale
- Brief description of how project will contribute to career advancement
- Literature Cited**:** References should be numbered in the sequence that they appear in the text. 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).

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: if the LOI is approved for full submission, the applicant will need to 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/

Submission

Prior to selecting "**Sign and Submit**", please complete a thorough review of the entire LOI. The "**Submit**" button will trigger validation on all required fields and identify any errors. Only the Principal Investigator will need to sign at the LOI stage. After selecting Submit, the applicant will receive an email asking them to sign the application FacePage electronically using Adobe Sign.

X. Full Application Guidelines

Full Application Deadline: Tuesday, November 14th, 2023 at 5:00 PM (EDT)

A Letter of Intent (LOI) must have been submitted and approved prior to receiving an invitation to proceed with a Full Application

Applications must be submitted online at https://awards.cff.org

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 awards.cff.org, the system will compile them into a single PDF file. You may preview this file by selecting "Application Full Print", as well as exporting the compiled PDF file.*

To login, please visit: https://awards.cff.org

If the LOI submission is approved to proceed to a full application submission, the application will have already been pre-loaded in the system. Log in with your existing credentials to access the application.

Your draft application will by listed under "**My Applications**", then within the "**Draft Applications**" section. Upon locating the draft application, you may select it to begin your submission.

Applicants may stop at any point but must click the **"Save"** button before exiting in order to save their progress.

The following sections are displayed as tabs across the application screen. Click on each section and follow the directions. Click "**Save**" as you complete each section.

Please note: Only select the "**Submit to AIO**" button after the application has been fully completed. This will trigger validation on all required fields and send the application to your Authorized Institutional Official "AIO" for review and signature.

GENERAL

Enter the title of your project, enter the project start and end dates, select the number of periods being requested, and complete any additional questions. Also, please complete the organizational assurances indications (i.e. IRB approval letter and status at the time of submitting the application) in this section.

Please note: If the applicant is new to CF research, Letters of Support and/or Collaboration should be provided and uploaded as Appendices.

***Please ensure that you review and comply with the Organizational Assurances and Certifications as cited below.**

CONTACT PROFILE

If a profile was completed during the LOI, the fields in this section will already be populated with the information entered in your Professional Profile. If you need to make any changes, you may update your profile in this section.

Once updated you must "**Save and Validate**" prior to returning to continue your submission

INSTITUTION

If a profile was completed upon registration, the applicant's/principal investigator's institution will be pre-loaded as the Lead Institution. Domestic applicants must verify their institution by entering the Employer Identification Number (EIN) or Tax Identification Number (TIN) to search the system for the correct institution. **Please be sure to use the dash formatting when entering your EIN/TIN (XX-XXXXXXX).** If the EIN/TIN is not located, you may add the legal institution. Please also confirm if the project site is the same as the legal institution.

Verification of Applicant Institution's Tax Status (upload as PDF documents):

The CFF GCMA 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 GCMA Office.

International Applicants (if applicable):
Not Applicable for this Program

CONTACTS

Please note: The INSTITUTION tab must be completed prior to adding internal contacts to ensure that the contacts are properly associated with the applicant institution.

If added during the LOI, this will be pre-populated but can be changed during the full application. Complete the required contact fields by searching by name for existing contacts at your institution for each role. If the desired institutional contact is not available in the system, you may select "**Add Internal Contact**" to create a basic contact profile in order to add the individual to your application.

Additional contacts not associated with the applicant institution may also be added. These contacts are considered additional contributors involved in the proposed research plan. These may include consultants, collaborators, or subcontractors. In order to add contacts external to the applicant institution, please select the appropriate "Add Subcontractors" or "Add Consultants/Collaborators" button(s) and add the contacts in the table, then click "Save".

REFERENCES

Letters of Reference for junior investigator investigators must be submitted by the following individuals:

- **The Chair of the applicant's department at the applicant Institution** – The letter of reference from the Department Chair should indicate the release of sufficient space and facilities for the work described, as well as guarantee the time commitment of the investigator to the project. If the applicant is currently a fellow, the letter of reference should include confirmation of the pending faculty-level appointment or other sources of support to ensure completion of the proposed project.
- **At least two other individuals with an established research career** familiar with the applicant's scientific interests and abilities. These references may be submitted by individuals outside the applicant's academic department or institution.

Letters of Reference must be submitted prior to submission of the application. To invite Referees, go to the "**REFERENCES**" tab of the online application, then select the blue button to open a pop-up window in order to add the referees in the table. Once you click "Save" and close the pop-up window, the referees will be sent an e-mail asking them to Accept or Decline the invitation to submit a letter of reference and will be provided instructions to submit the letter. **The applicant will be alerted if a referee Declines the invitation; please make sure to check this tab regularly to see the status of the references.** The applicant should inform Referees to submit the letters at least one (1) week prior to the application deadline. This helps to ensure that the letters have been uploaded before the application is submitted. Once the application has been submitted, no documents can be added.

Letters uploaded to http://awards.cff.org should not be password protected or otherwise encrypted. Such encryption will cause errors in assembling a single-print PDF of the application. The applicant should inform the individuals writing letters to not include password protection on their documents.

***Senior investigators, or those who have received a prior CFF/CFFT Research Grant or NIH equivalent, are not required to submit Letters of Reference; however, if they are new to CF research, Letters of Support and/or Collaboration should be provided and uploaded as Appendices.**

ABSTRACTS/RELEVANCE

In the space provided online for each abstract, 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:

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  Provide a statement of no more than 3,000 characters (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.

BUDGET

Select the "**Edit Budget**" button under Application Budget, to enter and begin completion of the application's budget detail for each year of funding being requested. Awards funded through this RFA are for a maximum of two (2) years.

- For collaborative research, the cumulative budget **may not exceed $150,000 per year in direct costs (plus 12% indirect costs) for up to 2 years**. This amount is inclusive of the cost of any subcontracts. If the lead site is collaborating with another center within their same institution, a single detailed budget is to be submitted in the Grants Management System for each year requested. If the collaboration is with an external institution (performing part of the proposed aims), this would be budgeted as a subcontractor.
- No primary data collection activities will be funded under this grant mechanism.
- Separate professional fees for interpretation of data (e.g., from X-rays, lab tests, PFTs) may not be included when such interpretation is performed by the named investigator(s), co-investigator(s), or consultants as part of the project, other than in exceptional circumstances. In such cases, justification for these fees must be described in detail in the budget justification template.

The following budget categories are offered under this program:

Salaries & Benefits - List the names, positions, and percent effort of all professional and non-professional personnel involved in the project, whether or not salaries are requested. 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 **$212,100**. 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 – (Honoraria/consultant fees for patient/family partners/advisors) - Patients and families involved in the development or evaluation of the proposed projects should be offered reimbursement for their participation. Budget should include patient/family roles, but it is not necessary to include individual names.

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 CF Foundation Grants and Contracts Office. Travel expenses may not exceed **$2,000 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."

Consumable Supplies - Itemize supplies e.g. test kits, devices, packing materials, etc., in separate categories and give the estimated cost of each category.

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.

Other Expenses - Itemize other expenses by major categories, such as duplication costs, graduate student tuition, publication costs, minor equipment (under $5,000), shipping expenses, computer charges, conference registration fees, etc.

Patient Research Costs – (Project-Related Patient/Family Costs) **–** No funds may be requested for patient costs specifically related to the proposed project.

Subcontractors Summary – If applicable, detailed budgets and budget justifications for each subcontract, including indirects, must be provided for each year of support. Subcontractors are added in the prior section entitled **CONTACTS**. The lead/prime applicant (PI) and/or Grants Officer can initiate/complete the subcontract budget. After adding Subcontractor(s), in order to access the subcontract budget activity, please select the "**BUDGET**" tab of the application and click the "Open" button next to each listed subcontractor. After completing the subcontract budget activity, please select "**Pending PI Acceptance**", as well as "**Submit**" to ensure the subcontractor budget is included as part of the main application budget.

For applications that include a subcontract with a third party, the applicant may request indirect costs on the first $25,000 of each subcontract per project period. Negotiations of subcontracts are between the applicant institution and the subcontractor.

Budget Detail – Indirect Costs

Indirect costs of up to twelve percent (12%) may be requested from CFF. Indirect costs may be requested for all expenses except for the following:

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

LOI UPLOADS

This section will allow access to the documentation uploaded at the LOI stage.

FULL APPLICATION UPLOADS

Download the available templates applicable to the project, upload the completed templates in PDF format to the corresponding attachment types within this section. Templates available for download include:

- Research Plan
- Critique Response (LOI)

- Collaboration Details
- Budget Justification
- Biographical Sketches of Key Personnel
- Other Support
- Facilities Available
- CFF Patient Registry Data Request (if applicable)

Research Plan (template available for download)

- Key figures and legends must be included in the Research Plan. If uploaded as Appendices, they will NOT be reviewed.
- At the top of each page, type the PI's name. Each page must be sequentially numbered at the bottom.
- Research Plans are limited to eight (8) 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.
    a. **Specific Aims:** State concisely and realistically the intent of the proposed project and the specific aim(s). Do not exceed one page. The focus of applications should be aligned with the mission of the CF Foundation: 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.
    b. **Background and Significance**: Briefly describe the background of the present proposal. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this project by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to advance remote monitoring in the real-world CF clinical care setting.
    c. **Preliminary projects/studies**: Summarize any preliminary work pertinent to this application that has been undertaken by the Principal Investigator(s) and/or information that will establish the competence and/or experience of the investigator(s) to pursue the proposed project.
    d. **Design and Methods**: Provide a detailed discussion of the project design and methods to be used to accomplish specific aims. Please discuss study aims. Provide a description of quality improvement or implementation science methodology and application to address project aims. Describe care algorithms/protocols or interventions to be tested. Discuss your proposed process and outcome measures of interest, data collection and analyses, and if applicable use of improvement charts (run and control charts, p-charts). Include a timeline for full project and if applicable, plan and frequency of testing, tracking cycles of change and reporting progress across sites.
    e. **Limitations, Broad Applicability, Sustainability, Spread and Scale:** Discuss potential difficulties and/or limitations of the proposed approach to achieve aims. Point out potential opportunities for broad applicability and sustainability. Discuss potential for spread and scale across the CF care center network.
    f. **Literature Cited**: References should be numbered in the sequence that they appear in the text and listed at the end of the Project 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).

Critique Response to LOI (template available for download)

Provide a point-by-point response to the limitations noted in the critiques of the LOI, using the template provided (three-page limit).

Collaboration Detail Template (template available for download, if applicable)

On the provided template please list each collaborator, including their institute and responsibilities or resources they are dedicating to the project.

Budget Justification (template available for download)
Describe costs listed in the Budget Detail. Use major categories, such as Salary & Benefits, Consultant Costs, Supplies, 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.

Biographical Sketches for 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. (CF Foundation 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.

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 CF Foundation 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.

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 space, 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.

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: if the LOI is approved for full submission, the applicant will need to 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/

Appendices (upload as PDF documents)
Appendices are restricted to the following three (3) categories*:

- Signed Letters of Support and/or Collaboration: A Letter of Collaboration from all Co-PIs or consultants should be uploaded and included in the application.
    - For junior investigators: Letters of support should be provided from the applicant's Department Chair and two mentors with established research careers (Associate Professor level rank (or equivalent) or higher).
- Certification of IRB approval if available at the time of application.
- Up to three (3) reprints of the applicant's work relating to the general area of improvement and innovation in the proposal may be uploaded in PDF format.

***No other types of Appendices will be reviewed.**

***Organization Assurances & Certifications**

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

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

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

Validation and Submission

Prior to selecting "**Sign & Submit to AIO**", please complete a thorough review of the entire application. The "**Sign & Submit to AIO**" button will trigger validation on all required fields and identify any upload errors or incomplete fields. Upon selecting Sign & Submit to AIO, the ability to edit the application will be locked pending review and approval by your AIO.

After selecting **Sign & Submit to AIO**, the applicant will receive an email asking them to sign the application Face Page electronically using Adobe Sign. Once signed by the PI, the Face Page will then be routed to the AIO contact that is listed on the application for review and signature.

To ensure the application is fully signed and submitted ahead of the Application Deadline for this program, please be sure to complete the application, and begin the Sign & Submit to AIO process in advance of the deadline.

XI. Other Information

Not applicable to this RFA

XII. Contact Information

For technical support and program/content information:
Primary CF Foundation Grants and Contracts contact Angela Minucci at aminucci@cff.org or 301-841-2614

For scientific questions:
Elizabeth Cromwell, PhD at ecromwell@cff.org

XIII. Electronic Application Checklist

LOI Submission Deadline: Wednesday, August 9th, 2023 at 5:00 PM (EDT)
Full Application Deadline: Tuesday, November 14th, 2023 at 5:00 PM (EDT)

Application must be submitted online at: awards.cff.org

LETTER OF INTENT

- ☐ LOI Project Description - (upload)
- ☐ Biographical Sketch(es) of Key Personnel (upload)
- ☐ CFF Patient Registry Data Request (upload, if applicable)

FULL APPLICATION

Face Page (upload) which includes:

- ☐ Signatures
  - ☐ Lead 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 Institution and PI Contact information, including correct mailing address - (online)
- ☐ Organization Assurances (check those that apply online)
  - ☐ Human Subjects Certification - Minimal patient risk only

Research Plan, Supporting Documents and Appendix:

- ☐ Abstracts ~ Summary of Relevance ~ Keywords - (complete online)
- ☐ Collaboration Detail (upload, if applicable)
- ☐ Research Plan - (upload)
  - ☐ Specific Aims
  - ☐ Background and Significance
  - ☐ Preliminary Results
  - ☐ Project Design and Methods
  - ☐ Limitations and Potential Pitfalls
  - ☐ Consultants/Collaborative Arrangements
  - ☐ Literature Cited (not included in Research Plan page limitation)
- ☐ Critique Response LOI - (upload, if applicable)
- ☐ Budget Detail for each year and for each subcontract, when applicable - (complete online)
- ☐ Budget Justification for each year and for each subcontract, when applicable - (upload)
- ☐ Biographical Sketches of Key Personnel - (upload)
- ☐ Other Support for all key personnel (NIH Format) - (upload)
- ☐ Facilities Available - (upload)
- ☐ Results of Past and Current CFF/CFFT Support – (upload)
- ☐ Verification of Applicant Institution's Tax Status - (upload)
  - ☐ W-9
  - ☐ 501(c)3, IRS Form 147C or equivalent tax status letter
- ☐ Appendices - (upload as PDF documents, if applicable)
  - ☐ Signed Letter(s) of Support and/or Collaboration
  - ☐ Certification of IRB approval, or other applicable organization assurances documents such as IACUC and IBC Approval Letters, if available at the time of application
  - ☐ Up to three (3) reprints of the applicant's work relating to the general area of improvement and innovation in the proposal

References

1. Knapp EA, Fink A, Goss CH, Sewall A, Ostrenga J, Dowd C, et al. The Cystic Fibrosis Foundation Patient Registry. Design and Methods of a National Observational Disease Registry. Annals of the American Thoracic Society. 2016;13(7):1014-5.