Program Name: CFF Program for Clinical Trials in Organ Transplantation (CTOT) Ancillary Studies with Letter of Intent (LOI) 2022

Brief Program Overview/Description: The Cystic Fibrosis Foundation (CFF) and Clinical Trials in Organ Transplantation (CTOT-20) investigators aim to facilitate access of the unique and important resource of well-characterized specimens and clinical data collected and banked through the CTOT-20 and CTOT-Extension (CTOT-ES) studies to the broader lung transplant research community. **The CFF is requesting Letters of Intent (LOIs) for research projects that aim to use available specimens and/or clinical data to improve knowledge of Chronic Lung Allograft Dysfunction (CLAD) pathogenesis and explore new approaches to detection, prevention, monitoring or treatment of CLAD.** Research projects may address the endotyping and mechanistic understanding of CLAD, identification and validation of biomarkers for early detection and monitoring of CLAD, and discovery of potential therapeutic targets to prevent or treat CLAD. If planning a study that only uses CTOT data, applicants are welcomed to propose investigating lung transplant outcomes other than CLAD. The applicant will be required to partner with a CTOT investigator. *This is a one-time Request for Applications (RFA).*

Funding Amounts: Funding varies based on the type of proposal. Section III provides additional information.

- Hypothesis-generating or data-only research: Funding of up to **$50,000 per year for up to two (2) years**, plus twelve percent (12%) indirect costs may be requested.
- Hypothesis-based research using both specimens and data: Funding of up to **$100,000 per year for up to two (2) years**, plus twelve percent (12%) indirect costs may be requested.

Eligibility Requirements:

- United States residents and applicants from outside the United States are welcome to apply.
- Additional eligibility requirements can be found in Section IV below.

Key Dates:

Published	March 7, 2022
*LOI Submission Deadline	April 20, 2022
LOI Applicant Notified	early July 2022
*Full Application Deadline	August 23, 2022
Committee Review Date	late October 2022
Notification to Applicants	late November 2022
Earliest Project Start Date	January 1, 2023

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*We highly encourage all applicants 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) Office is able to assist all applicant with any potential system-related queries prior to the Application Deadline.

I. About the Cystic Fibrosis Foundation

The mission of the Cystic Fibrosis Foundation (CFF) is to cure cystic fibrosis (CF) and to provide all people with 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.

II. Program Overview

Cystic fibrosis is a common, life-shortening autosomal recessive disorder that affects approximately 100,000 individuals worldwide. Abnormal mucus production in the respiratory tract is the primary cause of morbidity and mortality in CF, but other organs are also affected including the pancreas, sweat gland, intestine, bile duct of the liver, and male reproductive system. CF is caused by dysfunction of a single gene, Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), which codes for a chloride (Cl-) channel at the apical membrane of epithelial cells. Over 2,000 variants of CFTR have been identified. Advances in clinical development of small molecule CFTR modulators resulted in four therapies that address the underlying cause of CF for specific CFTR variants. These highly effective modulators correct the folding of and/or potentiate the CFTR protein in approximately 90% of people with CF. Potential CFTR modulators are in development to treat people with rare CFTR mutations who currently have no treatment option. Despite these innovations in CF treatments, there is still an unmet need to improve the quality of life and life expectancy of patients with end-stage CF lung disease.

Lung transplantation is a treatment option for people with CF and advanced obstructive lung disease resulting from lung infections, inflammation, and progressive bronchiectasis. While the transplant surgery replaces the damaged lung, people with CF are susceptible to post-transplant lung infections due to complications of immune suppression, graft rejection, and chronic lung allograft dysfunction (CLAD) which impact long-term survival. Over the last decade in the United States, over 2,400 people with CF have received lung transplants, with approximately 200 to 250 CF transplants performed annually prior to the wide availability of highly effective CFTR modulators. However, post-transplant survival is suboptimal with a median survival of approximately 10 years. To address these issues, it will be necessary to better understand lung transplant biology and the mechanisms by which CLAD develops.

In 2016, the CFF started the CF Lung Transplant Initiative (CFLTI) including an Advanced CF Lung Disease Program to address the unmet needs of people with CF and advanced CF lung disease (ACFLD). The mission of this initiative is to improve the care and long-term outcomes of individuals with ACFLD by optimizing decision-making and access to lung transplantation and improving outcomes after lung transplantation. Towards this end, the CFF is supporting research investigating strategies for early detection and intervention of CLAD.

For this RFA, the CFF is partnering with Clinical Trials in Organ Transplantation (CTOT-20) investigators to facilitate access of well-characterized specimens and clinical data collected and banked through the CTOT-20 and CTOT-ES studies to the broader lung transplant research community. CTOT-20 (ClinicalTrials.gov NCT02631720), was a NIH (NIAID) funded prospective observational cohort study of 803 adult lung transplant recipients (102 were people with CF) from five North American centers that collected serial clinical data, patient reported outcomes, and biospecimens from the time of transplant onward over a median follow-up of approximately 2.5 years[1]. The overall objective of CTOT-20 was to examine chronic lung allograft dysfunction (CLAD) phenotypes and the clinical and biological risk factors for CLAD. CTOT-20 ended in 2019, however due to the time-dependent nature of CLAD development, extended follow-up was critically necessary to allow more patients to develop CLAD. In 2019 the CFF funded the CTOT-Extension

[1] Snyder LD, Belperio J, Budev M, et al. Highlights from the clinical trials in organ transplantation (CTOT)-20 and CTOT-22 Consortium studies in lung transplant. Am J Transplant. 2020; 20:1489–1494. https://doi.org/10.1111/ajt.15957

Study (CTOT-ES; ClinicalTrials.gov NCT04126746) expanding specimen collection for two additional years and clinical data collection into the future, thus supporting the continued growth of this unique and important resource for lung transplant researchers. The clinical data and biospecimens generated through CTOT-20 have supported a broad range of studies to date examining risk factors for acute allograft rejection, lung cell gene expression in the setting of acute rejection, elevations of lung CXCR3 chemokines in the setting of allograft injury, hyaluronan as a biomarker of acute rejection, and lung bile acid and other inflammatory biomarkers for CLAD.[2]

The goal of this RFA is to identify highly relevant projects that aim to **use available CTOT specimens and/or data in new ways to improve knowledge of CLAD pathogenesis and explore new approaches to detection, prevention, monitoring or treatment of CLAD**. **If planning a study that only uses CTOT data, applicants are welcomed to propose investigating lung transplant outcomes other than CLAD.** Areas of interest can be found in Section VI below. A limited number of LOIs that meet this criterion will be invited to submit full applications. Applications that do not specify how the project can benefit people with CF and/or are deemed nonresponsive will not be invited for a full application. The applicant will be required to partner with a CTOT investigator (list provided below) by either establishing a collaboration prior to LOI submission or having a collaborator assigned by the LOI reviewing committee, if invited to submit a full application.

Please note: This is a one-time RFA.

CTOT Data Information

Specimens	Details
Bronchoalveolar lavage (BAL) Supernatant	Collected during each clinically performed bronchoscopy
BAL Cell Pellet	
Plasma	Collected longitudinally at pre-specified timepoints (generally pre-Tx, post-Tx M1, M3, M6, M9, M12 and Q6 months thereafter) throughout the subject's study participation and at the time of all clinically performed bronchoscopies
Serum	
DNA	
RNA	

[2] ▪ Todd J.L., Neely M.L., Kopetskie H., et al. Risk factors for acute rejection in the first year after lung transplant. A multicenter study. Am J Respir Crit Care Med. 2020; 202: 576-585. https://doi.org/10.1164/rccm.201910-1915OC

▪Shino MY, Li N, Todd JL, Neely ML, Kopetskie H, Sever ML, et al. Correlation Between BAL CXCR3 Chemokines and Lung Allograft Histopathologies: A Multi-Center Study. Am J Transplant. 2021 Oct;21(10):3401-3410. https://doi.org/10.1111/ajt.16601

▪ Hostetler, Haley P. MD1; Neely, Megan L. PhD2,3; Kelly, Francine L. PhD1; Belperio, John A. MD4; Budev, Marie MD5; Reynolds, John M. MD1; Shah, Pali D. MD6; Singer, Lianne G. MD7; Snyder, Laurie D. MD1,3; Palmer, Scott M. MD1,3; Todd, Jamie L. MD1,3 Intragraft Hyaluronan Increases in Association With Acute Lung Transplant Rejection, Transplantation Direct: 2021 April;7(4):e685 https://doi.org/10.1097/TXD.0000000000001138

▪ Weigt SS, Wang X, Palchevskiy V, Li X, Patel N, Ross DJ, Reynolds J, Shah PD, Danziger-Isakov LA, Sweet SC, Singer LG, Budev M, Palmer S, Belperio JA. Usefulness of gene expression profiling of bronchoalveolar lavage cells in acute lung allograft rejection. J Heart Lung Transplant. 2019 Aug;38(8):845-855. https://doi.org/10.1016/j.healun.2019.05.001

▪ Zhang CYK, Ahmed M, Huszti E, Levy L, Hunter SE, Boonstra KM, Moshkelgosha S, Sage AT, Azad S, Zamel R, Ghany R, Yeung JC, Crespin OM, Frankel C, Budev M, Shah P, Reynolds JM, Snyder LD, Belperio JA, Singer LG, Weigt SS, Todd JL, Palmer SM, Keshavjee S, Martinu T; CTOT-20 investigators. Bronchoalveolar bile acid and inflammatory markers to identify high-risk lung transplant recipients with reflux and microaspiration. J Heart Lung Transplant. 2020 Sep;39(9):934-944. https://doi.org/10.1016/j.healun.2020.05.006

CTOT Specimen Information

Data	Details				
Bronchoscopy	Date	Findings	Surveillance/For Cause	Other Procedures performed	
Microbiology (lower respiratory)	Date	Fungus/Bacteria/Mycobacteria/Virus			
Transbronchial biopsy/Wedge	Date	Location	Rejection pathology/Additional pathology/Infectious organisms		
Quantitative BAL Fluid Cell Differential (4 sites)	Date	Cell type % (Neutrophils/Eosinophils/Lymphocytes/Macrophages/Monocytes/etc)			
Native Lung Disease	Specific disease (primary and secondary) and United Network for Organ Sharing (UNOS) grouping				
Transplant Surgical Details	Date	Ex-vivo lung perfusion (EVLP), primary graft dysfunction (PGD), Induction, extracorporeal membrane oxygenation (ECMO)/cardiopulmonary bypass (CPB), other surgery			
Cytomegalovirus (CMV) PCR (quantitative)	Date	All results (transplant center and external results)			
Pulmonary function test (PFTs)	Date	All forced vital capacity (FVC), forced expiratory volume in first second (FEV1) results (transplant center and external results)			
Donor-specific antibody (DSA)	Date	DSA specificity			
Posttransplant lymphoproliferative disorder (PTLD)/Malignancy (CTOT-ES only)	Date of Diagnosis	Treatment	Location of malignancy/PTLD		
COVID - positive tests (CTOT-ES only)	Date of positive test	Specimen source & Test type	Symptoms yes/no	Hospitalized yes/no	
Death/Re-transplant	Date	Cause of death or retransplant (question about whether COVID a factor included in CTOT-ES)			
CMV Medications	Yes\No during specified interval	Drug Name	Stop date	Reason for stopping	
Investigational drugs taken	Date	Sponsor	Study Name		
Intravenous immune globulin use	Yes\No during specified interval				
Augmented immunosuppression	Start date	Drug Name			
Maintenance immunosuppression	Yes\No during specified interval	Drug Name			
Gastroesophageal reflux disease (GERD) testing	Date	Test type	Normal/Abnormal		
Patient-Reported Outcomes (Short Form – 36, St. George's Respiratory Questionnaire)	Date	Results			
CLAD	Onset Date	Phenotype	Probable/Definite	Imaging findings around PFT decline	
UNOS Data	Donor info, typing	Recipient info, typing	Hosp length of stay	CMV/ Epstein-Barr Virus (EBV)	LAS
Human leukocyte antigen (HLA) Data	Date	Mean fluorescence intensity			
Pre-transplant Frailty (n=148)	Fried Frailty Phenotype	Cumulative Frailty Index			

III. Funding Amounts

- Hypothesis-generating or data-only research: Funding of up to **$50,000 per year for up to two (2) years**, plus twelve percent (12%) indirect costs may be requested.
- Hypothesis-based research using both specimens and data: Funding of up to **$100,000 per year for up to two (2) years**, plus twelve percent (12%) indirect costs may be requested.
- 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
- Research supplies
- Equipment
- Research-related subject costs
- Consultant costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for scientific/technical meeting(s)

Direct costs for the following are unallowable:

- Tuition

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

- Equipment (items over US $5,000 in value)
- Computer software
- Software licenses

***Applicants may request indirect costs on the first $25,000 of each subcontract for the project period.**

IV. Eligibility Requirements

- United States residents and applicants from outside the United States are welcome to apply.
- Applicants must be independent investigators.
- Applicants will be required to partner with a CTOT investigator by either establishing a collaboration prior to LOI submission or asking that a collaborator be assigned by the LOI reviewing committee (if invited to submit a full application).
- Applicants must hold faculty level positions. Fellows may submit applications; however, funding will only be considered if they will hold a faculty-level appointment at the time of the award.
- Applicants must be a M.D., D.O., Ph.D., or dual M.D./D.O., Ph.D. scientist.
- Collaboration with PhD Biostatistician is strongly encouraged for clinical and translational projects to ensure feasibility and rigor of the proposed analysis
- 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 lungtransplant@cff.org.

V. Mentorship Requirements

Not applicable to this RFP

VI. Goals of Research Currently of Interest to CFF CF Lung Transplant Initiative/Priority Areas

The objective of this RFA is to fund highly meritorious research projects that use available CTOT specimens and/or data to improve lung transplant outcomes, knowledge of CLAD pathogenesis, and explore new approaches to detection, prevention, monitoring or treatment of CLAD. Areas of interest include, but are not limited to:

- Improving the understanding of CLAD endotypes, particularly defining mechanisms underlying the development of obstructive, restrictive, or mixed CLAD
- Defining pathogenesis of CLAD with the goal of identifying new therapeutic targets
- Identifying and/or validating physiologic or imaging techniques or biomarkers for early diagnosis and/or monitoring of CLAD
- Applying advances in lung transplant immunology and mechanisms of fibrosis to the identification and/or validation of biomarkers and therapeutic approaches to prevent or treat CLAD
- Identifying differences in relevant transplant outcomes, including acute rejection, infections, renal dysfunction, malignancies and CLAD, in CF lung transplant recipients
- If planning a study that only uses CTOT data, applicants are welcomed to propose investigating lung transplant outcomes other than CLAD
- Projects may combine the use of CTOT data with available specimens collected through other efforts

A goal of this RFA is to promote collaboration between applicants and CTOT investigators such as:

- Principal Investigator: Scott M Palmer, MD, MHS, Duke University
- Study Chair: John Belperio, MD, University of California, Los Angeles
- Co-I: Laurie Snyder, MD, Duke University
- Co-I: Jamie Todd, MD, Duke University
- Co-I: Stephen (Sam) Weigt, MD, University of California, Los Angeles
- Pali Shah, MD, Johns Hopkins University
- Lianne Singer, MD, United Health Network, Toronto
- Marie Budev, DO, Cleveland Clinic
- John Reynolds, MD, Duke University

VII. Review and Award

Applications will be reviewed and scored by a CFF ad-hoc review committee that includes CTOT investigators. 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 CFF project portfolio. The committee will prioritize research that is novel, impactful, feasible within the scope of the award, makes efficient use of the clinical data and/or biological samples, and is non-redundant with existing or ongoing CTOT analysis. All awards are subject to compliance with applicable regulations and CFF policies and are contingent upon the availability of CFF funds.

Proposals should clearly demonstrate how the research will advance our understanding of transplant biology and outcomes of lung transplantation for individuals with CF.

Applications will be evaluated on the following:

- Relevance to the priority areas stated above
- Scientific merit of the project as described in the applicant's Research Plan
- PI's background and experience
- Adequate facilities and research environment for the project
- Collaboration with CTOT investigator
    - How the individual applicant fits within the larger CTOT and CTOT-ES studies
    - Synergy between the applicant and CTOT investigator
    - Value added from the collaboration
    - How individual applicants will communicate and collaborate (e.g., sharing reagents, specimens and data)
    - Consultant arrangements and/or collaborations (if any) with other investigators outside the applicant's group

Low priority scores in the reviews commonly result from the following shortcomings of the application:

- Failure to address the evaluation criteria described above
- Insufficient information or documentation
- Inadequate statement of hypotheses, experimental design, or methods
- Failure to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the proposed research
- Insufficient or improper controls
- Failure to describe potential relevance of the proposed study to issues in lung transplantation for CF
- 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 (e.g., airway epithelial cells)
- Inadequate description of how the collaboration will be executed.
- Failure to consider overlap with previous or ongoing CTOT studies (Please refer to ***Section XI. Other Information*** below for a full list of completed and ongoing analyses)
- Failure to adequately address sample size and power
- Requirement for sample types or clinical data not available within the CTOT or CTOT-ES

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

Awardees are required to provide CFF 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. CFF 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 lungtransplant@cff.org for approval prior to submitting the application. Contact information for technical questions is provided below.

General Timeline:

Published	March 7, 2022
*LOI Submission Deadline	April 20, 2022
LOI Applicant Notified	early July 2022
*Full Application Deadline	August 23, 2022
Committee Review Date	late October 2022
Notification to Applicants	late November 2022
Earliest Project Start Date	January 1, 2023

*We highly encourage all applicants 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 GCMA

Office is able to assist all applicant with any potential system-related queries prior to the Application Deadline.

IX. Letter of Intent Guidelines

LOIs Submission Deadline: Wednesday April 20, 2022 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" or "International Institution" options to ensure that your profile aligns properly with the institution 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 "**CFF/Clinical Trials in Organ Transplantation (CTOT) w/LOI 2022**" 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, IACUC, and/or IBC/rDNA 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

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. You may find your EIN by referencing the Institutional W-9 or equivalent documentation. If the EIN/TIN is not located in our system, you have the option to 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.
- Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.

International Applicants (if applicable):

For international applicants, you will need to answer an eligibility question specifying if you are an independent investigator. If answering yes, CFF may require an additional letter of support to be added to the application to verify eligibility.

Applicants whose institution is not a United States based-entity will be contacted to provide additional information and completion a CFF International Institution Form. The completion of this form also includes submission of the following documentation:

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

Applicants who have provided these documents within the past one (1) year are not required to resubmit them. However, if any of the above documents have been updated since they were previously submitted, please upload any updated documents. The CFF GCMA Office will contact applicants if documents are outdated or missing.

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

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 co-mentors, consultants, collaborators, or subcontractors. If the desired external contact is not available in the system, you may select "**Add External Contact**" to create a basic contact profile in order to add the individual to your application.

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:

- **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**: 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.

  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 CFF/Clinical Trials in Organ Transplantation (CTOT) w/LOI 2022 program are awarded for a maximum of two (2) years, up to:

- $50,000/year in direct costs (plus an additional 12% indirect costs) for hypothesis-generating or data-only research.
- $100,000/year in direct costs (plus an additional 12% indirect costs) for hypothesis-based research using both specimens and data.

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

LOI UPLOADS

Download the **LOI Project Description** template, and upload the completed template in PDF format providing, at a minimum, the Hypothesis, Specific Aims, Significance, and Expected Outcomes **(maximum of three (3) pages not including the literature cited).** Components should include:

- Descriptive title of the proposed research
- Clear rationale for the project, including expected significance of the project for the CF and lung transplant community and how it advances the CFF mission
- Hypothesis and specific aims
- Brief overview of proposed research design/approach
- Assurances that the required laboratory biosafety equipment/facilities are available to perform the studies

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).

***Note**: If applicable, funding is contingent upon approval and ability to access clinical specimens and/or data.*

Submission

Prior to selecting "**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 Face Page electronically using Adobe Sign.

X. Full Application Guidelines

Full Application Deadline: Tuesday, August 23, 2022 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, IACUC, and/or IBC/rDNA 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 on page 21.**

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. You may find your EIN by referencing the Institutional W-9 or equivalent documentation. If the EIN/TIN is not located in our system, you have the option to 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.
- Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.

International Applicants (if applicable):
For international applicants, you will need to answer an eligibility question specifying if you are an independent investigator. If answering yes, CFF may require an additional letter of support to be added to the application to verify eligibility.

Applicants whose institution is not in the United States will be contacted to provide additional information and completion a CFF International Institution Form. The completion of this form also includes submission of the following documentation:

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

Applicants who have provided these documents within the past one (1) year are not required to resubmit them. However, if any of the above documents have been updated since they were previously submitted, please upload any updated documents. The CFF GCMA Office will contact applicants if documents are outdated or missing.

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

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 co-mentors, consultants, collaborators, or subcontractors. If the desired external contact is not available in the system, you may select "**Add External Contact**" to create a basic contact profile in order to add the individual to your application.

REFERENCES

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 OR is within their first five years of their first academic appointment at the level of Assistant Professor or equivalent. Letters of Reference for junior 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.

- **At least two other individuals** familiar with the applicant's scientific interests and abilities.

Letters of Reference must be submitted prior to submission of the application. The applicant should inform Referees that letters need to be submitted 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. To invite Referees, go to the "**REFERENCES**" tab of the online application, and first search for the referee using the lookup field. If the referee is not located in the system, you may select "**Add Referee**" to create a basic contact profile in order to add the individual to the application. Once added, this will generate automated emails (with instructions) that will be sent to each Referee. **The applicant will not be alerted when a reference is completed or declined; please make sure to check this tab regularly to see the status of the references.**

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.**

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:

- **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**: 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.

  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 hypothesis-generating or data-only research, the budget **may not exceed $50,000 in direct costs per year (plus 12% indirect costs) for a maximum of two (2) years.** This amount is inclusive of the cost of any subcontracts.
- For hypothesis-based research using both specimens and data, the budget **may not exceed $100,000 per year in direct costs per year (plus 12% indirect costs) for a maximum of two (2) years.** This amount is inclusive of the cost of any subcontracts.
- If a 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 both years. If the collaboration is with an

external institution (performing part of the proposed aims), this would be budgeted as a subcontractor.

- Services that are part of routine medical care (as defined by the U.S. Department of Health and Human Services) may not be included in the project budget. Whenever possible, the price of services (e.g., X-rays, EKGs, PFTs, etc.) provided by the institution should be negotiated to the lowest possible non-profit price.
- 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.
- Under most circumstances, hospitalization costs of study subjects cannot be included in this budget.

The following budget categories are offered under this program:

Salary & 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 **$203,700**. 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. Qualifying consultants are individuals that are generally not employed at the applicant institution and/or are consulting independently to the project.

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 GCMA 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. glassware, chemicals, animals, in separate categories and give the estimated cost of each category. If animals are involved, state the number, unit purchase cost, and unit care cost.

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, publication costs, minor equipment (under $5,000), computer charges, conference registration fees, etc. Tuition costs may be requested for personnel supported through this study but may not exceed **$10,000** per person per year.

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)).

Subcontractors Summary – If applicable, detailed budgets and budget justifications for each subcontract, including indirect costs, 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 "External Requests" tab near the top right of the screen and navigate to the subcontract activity to complete the entry. 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 (12) percent may be requested from CFF. Indirect costs may be requested for all expenses except for the following:

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

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:

- Collaboration Detail Template (required for collaborative research only)
- Research Plan
- LOI Critique Response
- Budget Justification
- Biographical Sketches of Key Personnel
- Other Support
- Facilities Available
- Results of past and current CFF/CFFT Support
- CFF Patient Registry Data Request Application (if applicable)

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

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

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 twelve (12) 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. Hypotheses and Specific Aims:** State concisely and realistically the intent of the proposed research and the hypothesis to be tested. Do not exceed one page. The focus of applications should be aligned with the mission of the Cystic Fibrosis 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 research by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF and lung transplantation. In addition, the applicant should describe the relationship of the proposed work to his/her/their long-term career goals. Preference will be given to those applicants who have an interest in a long-term career in CF-related lung transplantation research.
  - **c. Preliminary 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 study.
  - **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; sample size estimates*; description of experimental procedures and schedule including a study time-line for full project; quality control; and a description of your proposed data analysis and statistical procedures for your hypothesis testing. If applicable, provide study details including but not limited to: subject enrollment (including age range), pubertal status, sex distribution and eligibility criteria. 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, data and/or specimens.
  - **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 data and/or material required by this award is to be furnished by other individuals, include a statement from these individuals agreeing to their participation and precautions taken to ensure anonymity of patients.
  - **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).

Critique Response (template available for download, if applicable)
Provide a point-by-point response to the limitations noted in the critiques of the LOI, using the template provided.

Budget Justification (template available for download)
Describe costs listed in the Budget Detail. Use major categories, such as Salary & Benefits, Consultant Costs, Major Equipment, etc. Justify all items and make sure amounts and figures listed in the narrative are consistent with those listed in the Budget Detail.

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. (CFF defines "key personnel" as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project.) Do not exceed five (5) pages per person.

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.

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.

Results of Past and Current CFF/CFFT Support (template available for download)
Identify the results of past and current CFF/CFFT support (e.g., subsequent funding from other sources, journal articles, and invited presentations) and the CFF/CFFT award from which they resulted for the past five years. Please note that the following information must be included with each research project identified:

- CFF/CFFT Award #
- Principal Investigator (PI)
- CFF/CFFT Project Title
- Applicant's Title on Project
- Project Start/End Dates
- Total CFF/CFFT Award Amount
- Results of Support

CFF Patient Registry Data Request (download available, upload if applicable)
Researchers who wish to request Registry data must complete and submit the "Application for CFFPR Data and Confidentiality Agreement" application to datarequests@cff.org prior to submitting their full application to CFF. The formal application for CFF Patient Registry Data Requests can be found at https://www.cff.org/Research/Researcher-Resources/Tools-and-Resources/Patient-Registry-Data-Requests/

Note: *The application must be submitted using the online system available from the link above and the email from the system indicating receipt of the application must be uploaded to the submission. Funding is contingent upon approval to access registry data.*

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 Co-PIs, if any, should be uploaded and included in the application. Investigators new to CF research are required to consult/collaborate with an established CF investigator/clinician either at their own institution or another. The letter from the collaborator/consultant should be explicit as to how the proposed work is relevant to CF and how he/she will assist the investigator new to CF research.
  Note: Junior investigators must provide such letters by contacting referees via section #6 of the navigation bar.
- 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 research 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 GCMA 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 GCMA 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 GCMA 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.

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

CTOT-20 Specimen Types used and Analyses Performed
Completed and Ongoing

Analysis performed	Specimen	Additional specimen	Outcome of interest	Cohort
Multiplex chemokines/cytokines	BAL	N/A	Allograft injury and CLAD	Subset CTOT patients
Hyaluronan	BAL	Blood	Allograft injury and CLAD	All CTOT patients
Cell free DNA (cfDNA)	BAL	Plasma	Allograft injury and CLAD	Subset CTOT patients
Mulitplex cytokine	Serum	N/A	Frailty, Primary Graft Dysfunction, Allograft injury, CLAD and Death	Subset CTOT patients
Antibody characteristics - titer/ mean fluorescence intensity (MFI)/avidity/IgG subclass	Serum	N/A	Allograft injury/CLAD/response to Antibody therapy	Subset CTOT patients
Club Cell Secretory Protein (CCSP)	BAL	N/A	Allograft injury and CLAD	Subset CTOT patients
RNA Seq	BAL cell pellet	N/A	Allograft injury and CLAD	Subset CTOT patients
Multiplex chemokines/cytokines	BAL	Plasma	Allograft injury and CLAD	Subset CTOT patients
microRNA (coding and non-coding RNA)	BAL cell pellet	N/A	Allograft injury and CLAD	Subset CTOT patients
T Cell Receptor profiling	BAL cell pellet	N/A	Allograft injury and CLAD	Subset CTOT patients
Proteomics, metagenomics, cfDNA	Plasma	N/A	Allograft injury and CLAD	Subset CTOT patients
Peripheral blood RNAseq	Blood	Paxgene	Allograft injury and CLAD	Subset CTOT patients

CTOT-20 and CTOT-ES Data Analyses
Completed and Ongoing

Analysis	Cohort
Clinical risk factors for CLAD	All CTOT patients
Risk factors for acute rejection and lymphocytic bronchiolitis (LB) in first post-transplant year	First 400 patients
Risk factors for organizing pneumonia and acute lung injury in first post-transplant year	First 400 patients
Association of eosinophils in the BAL with CLAD	All CTOT patients
Determinants of Quality of Life within first year after transplant	All CTOT patients
Risk factors for cytomegalovirus infection after transplant	All CTOT patients
Pulmonary function test trajectory, CLAD phenotype, and survival after CLAD onset	All CTOT patients

XII. Contact Information

For technical support and program/content information:
Primary CFF GCMA contact Erik Warnke at ewarnke@cff.org or 301-841-2667

Secondary CFF GCMA contact Edwin Gregorian at egregorian@cff.org or 301-841-2614

For scientific questions:
lungtransplant@cff.org

XIII. Electronic Application Checklist

LOI Submission Deadline: Wednesday, April 20, 2022 at 5:00 PM (EDT)
Full Application Deadline: Tuesday, August 23, 2022 at 5:00 PM (EDT)

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

LETTER OF INTENT

- ☐ LOI Project Description - (upload)

FULL APPLICATION

Face Page (upload) which includes:

- ☐ Signatures
  - ☐ Principal Investigator (Co-PI's are not required to sign)
  - ☐ The Official authorized to sign on behalf of the Applicant Institution
- ☐ Applicant/PI information - (online)
- ☐ Complete 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 Involving recombinant or synthetic nucleic acid molecules information
  - ☐ Research Involving Animals information

Research Plan, Supporting Documents and Appendix:

- ☐ Abstracts ~ Summary of Relevance ~ Keywords - (complete online)
- ☐ Collaboration Detail (upload, if applicable)
- ☐ Research Plan - (upload)
  - ☐ Hypothesis and Specific Aims
  - ☐ Background and Significance
  - ☐ Preliminary Results
  - ☐ Experimental Design and Methods
  - ☐ Limitations and Potential Pitfalls
  - ☐ Consultants/Collaborative Arrangements
  - ☐ Literature Cited (not included in Research Plan page limitation)
- ☐ LOI Critique Response - (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)
- ☐ Letters of Reference for Junior Investigators - (invite referees to submit via awards.cff.org –*Note: applicant will not be able to see the letters)*
- ☐ CFF Patient Registry Data
  - ☐ Application for CFFPR Data and Confidentiality Agreement – (upload, if applicable)
- ☐ Verification of Applicant Institution's Tax Status - (upload)
  - ☐ W-9 (U.S. applicants) or W-8BEN-E (non-U.S. applicants)
  - ☐ 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 research in the proposal