CYSTIC FIBROSIS FOUNDATION

Screening Improvement Program (SIP) for Optimizing the Diagnosis of Infants Award

POLICIES AND GUIDELINES

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Application Deadline: April 2, 2018

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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 the disease the opportunity to lead full, productive lives by funding research and drug development, promoting individualized treatment, and ensuring access to high-quality, specialized care.

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

II. SCREENING IMPROVEMENT PROGRAM FOR OPTIMIZING THE DIAGNOSIS OF INFANTS AWARD OVERVIEW

The overall purpose of the Screening Improvement Program (SIP) is to catalyze efforts aimed at improving the screening system used for early diagnosis. This Request for Applications (RFA) is focused specifically on expediting the early diagnosis of CF through accelerated Newborn Screening (NBS). However, this RFA is not intended to support projects devoted to clinical trials/interventions.

Newborn screening programs have been organized as population-based public health services applying preventive medicine principles in defined regions to reduce morbidity and mortality from certain genetic disorders by pre-symptomatic detection of risk using dried blood specimens from newborns analyzed in central laboratories that are linked to clinical follow-up programs for diagnosis and rapid institution of specialized therapies. Their organization features a system of care that includes education, screening per se, follow-up, diagnosis, evaluation/management, and quality assurance. After demonstration of benefits and endorsement by both CDC and the CFF, the implementation of CF NBS during 2006-2009 throughout the USA has provided many new opportunities for enhanced care, teaching, and research, but also occurred with such relative rapidity that a need for quality improvement and assurance has become apparent. To that end, CFF has developed a Screening Improvement Program for Optimizing the Diagnosis of Infants. This program will provide Quality Improvement (QI) awards to leaders of US programs for projects designed to improve the early diagnosis of CF through the NBS system and/or the initial management of infants with positive screening tests and communications with their families.

The screening process involves a sequence of procedures that begins with collection of dried blood spot specimens on filter paper cards, which is usually accomplished in the birthing hospital at two to three days of age. These specimens are then sent to a regional NBS laboratory, which is typically the state's public health lab, where the analyses are either partially or completely performed; in some regions, a biomarker test is done in one site and a DNA analysis elsewhere. In addition, a second specimen may be needed when the initial blood spots are unsatisfactory or the screening algorithm requires a repeat analysis. The next step involves reporting results to a primary health care provider and/or CF center. Then, for positive screening results, a follow-up assessment needs to be organized through provider/parent communications, scheduling of a sweat test, and a diagnostic evaluation of the infant with successful sweat testing. In this

complex sequence, there are many possibilities of delays. Observations have shown that delays can occur in the dried blood specimen collection and/or transfer steps, in the laboratory analyses, in the procurement/transfer of second blood specimens, in the communications processes, and in scheduling and successful completion of sweat tests. Thus, **timeliness** of diagnosing CF through efficient NBS can be challenging. Although guidelines for CF NBS published by the Clinical and Laboratory Standards Institute state that t*he goal is for all infants with CF to be diagnosed and integrated into clinical care systems at CF clinics by two or three weeks of age,* data available in the CFF Patient Registry have revealed that many states seem to be experiencing delays and not routinely diagnosing CF through NBS during the neonatal period, i.e., the first 28 days of life. The CFF believes that the timeliness aspect of this care delivery challenge and all of the other components of the NBS system can be addressed by quality improvement projects.

Applicants are encouraged to refer to *The Standards for Quality Improvement Reporting Excellence* (SQUIRE 2.0) revised publication guidelines found at http://qualitysafety.bmj.com/content/qhc/25/12/986.full.pdf to see what is required for work on QI-focused projects to be published.

General Guidelines and Eligibility:

- All applicants must be U.S. citizens or U.S. permanent residents (i.e. applicants must have obtained permanent residency prior to the time of application)**.**
- Applicants must be actively engaged in CF NBS programs and involved in the second, third, and fourth components listed below:
  1. Education of professionals and parents
  2. Screening, i.e. specimen collection, submission, and testing
  3. Follow-up of abnormal and unsatisfactory test results
  4. Confirmatory testing and diagnosis
  5. Medical management and periodic outcome evaluation, including treatment monitoring
  6. System evaluation and quality assurance
- The applicant institution should have a Cystic Fibrosis Foundation-accredited Center or Affiliate program. The CF Center Director or Affiliate Director must provide a letter of support affirming that the applicant will be integrated into the CF Center. Each application should also engage the Director of the regional NBS Laboratory.
- Each application must describe the goals and framework for the project (including the NBS steps that need attention based on data presented in the application), the QI team and its structure, the designated leader and documentation of available time and commitment, a proposed timeline and meeting schedule that demonstrates the applicant's potential to complete the project in one to two years, and a willingness to share the findings/recommendations with all CF NBS programs and CF centers. Statewide QI proposals that engage the NBS lab and all regional CF centers will be considered. Efforts should be made, whenever possible, to incorporate the people served by NBS into the improvement work and identify "best practices."

- Successful applicants will receive funding of up to **$40,000 direct costs per year,** plus eight percent (8%) indirect costs, for one (1) year and may be eligible for up to two (2) years of funding. Funding for Year 2 will depend on the availability of funds and be subject to the submission and approval of a renewal progress report.

III. REVIEW AND AWARD

All applications are evaluated by a committee of reviewers. Funding of awards is based on the priority score awarded each application and the recommendations of reviewers. Relevance of the proposed project to issues in CF is also considered in determining awards. All awards are subject to observance of the regulations and policies of CFF related to that category of support and are contingent upon the availability of CFF funds.

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

IV. SUBMISSION INFORMATION & GENERAL TIMELINE

Application Deadline: Monday, April 2, 2018 at 5:00 PM (ET)

Submit online through proposalCENTRAL: https://proposalcentral.altum.com/
(Refer to Section V of these guidelines for specific submission instructions)

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

General Timeline

Application Deadline	April 2, 2018
Review by Committee	early June 2018
Notification to Applicants	June 15, 2018
Earliest Start Date for Awarded Projects	August 1, 2018

V. FULL APPLICATION GUIDELINES

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

Documents should be typed using:

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

***Note:** When all the documents have been uploaded to proposalCENTRAL, the system will compile them into a single PDF file in the correct sequence, in the correct sequence, as shown in Section*

VI. ELECTRONIC APPLICATION CHECKLIST. Page numbering is not necessary for all uploaded templates except as noted in the instructions for specific templates in this section.

Log-in at proposalCENTRAL: https://proposalcentral.altum.com/.

First-time applicants must register to create a user name and password for proposalCENTRAL and will need to complete a profile online before applying. If you are already registered and cannot remember your password, click on the **"Forgot Your Username/Password?"** link below the **"Application Login"** fields.

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

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

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

Locate the listing for the **"Screening Improvement Program (SIP) for Optimizing the Diagnosis of Infants"** program. Click on the **"Apply Now"** button in the column on the far right to open the application form.

Applicants may stop at any point, but must click the **"Save"** button before exiting in order to save their work. When logging in to continue, click on the blue tab, **"Manage Proposals",** and then the **"Edit"** button.

The following sections are listed in the navigation menu to the left of the application screen. Click on each section and follow the directions.

1. **Title Page:** Enter the title of your project and answer the required questions. Click the **"Save"** button.

2. **Download Templates & Instructions:** Download the available templates applicable to the project, fill them out and upload them when completed in Section #9. Templates available include: Biographical Sketches of Key Personnel, Other Support, Budget Detail, Budget Justification, Quality Improvement Project Plan, Facilities Available, and Appendices.

3. **Enable Other Users to Access this Proposal:** Complete this section online if you wish to designate access to another individual, such as an assistant who has registered on proposalCENTRAL. Enter the email address of the individual and in the **"Permissions"** column, use the pulldown menu to select the type of access you wish to give. Please note that only

delegates who are granted **"Administrator"** rights can submit applications on behalf of the applicant. Check the **"Auto Notify"** box and then **"Save".**

4. **Applicant/PI:** If a profile was completed upon registration, the fields in this section will already be populated with the information entered in your Professional Profile. If you need to make any changes, click the **"Edit Professional Profile"** button and follow the instructions. If a profile was not completed, enter the required information and click **"Save"**.

5. **Institution & Contacts:** If a profile was completed upon registration, the Principal Investigator's (PI) institution will be preloaded as Lead Institution. If a profile was not completed, enter the required information and click **"Save"**. Be sure to use the full legal name of the institution.

6. **Scientific & Lay Abstracts:** In the space provided online for abstracts, provide a statement of no more than 2,000 characters (including spaces) each explaining the subject of the QI proposal and its relationship to CF. Two different abstracts are required as follows:
   - **Lay Abstract:** This statement will be used to inform the non-scientific departments of CFF and the general public of the nature of this work. Applicants should not include any confidential or proprietary information, including intellectual property, in the lay abstract.
   - **Scientific Abstract:** This statement will be used to inform the scientific community.

7. **Budget Summary:** Fill in the start and end date and applicable amounts for the support requested by completing the applicable online fields (Period 1 and/or Period 2). The total budget requested cannot exceed $40,000 plus eight percent (8%) indirect costs per year.

   Note: *The Budget Detail and Budget Justification templates downloaded in Section #2 must also be completed for each year of support requested and uploaded in Section #9.*

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

9. **QI Project Plan & Supporting Documents:** In this section, upload the completed templates downloaded in Section #2 above in PDF format. Click on **"Attach Files"** and in the next screen select the attachment type from the pulldown menu, enter a description for the attachment in the corresponding field, choose the file to be uploaded, and drag and drop it as indicated in the online form. Click **"Upload and Continue"**. Do this for each attachment. Click the **"Back"** button when all required files have been uploaded to go back to the main screen.

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

A. BIOGRAPHICAL SKETCHES OF KEY PERSONNEL (template available online)

Complete and upload an NIH Biographical Sketch for all key project personnel, beginning with the Principal Investigator. (CFF defines "key project personnel" as any individual with an advanced degree that will play an instrumental role in the accomplishment of the project.) Do not exceed five (5) pages per person.

B. OTHER SUPPORT (template available online)

Complete and upload an "Other Support" form, for all key project personnel, beginning with the Principal Investigator. There is no page limitation.

C. BUDGET DETAIL AND BUDGET JUSTIFICATION (separate templates available online)

Fill out the Budget Detail and Budget Justification templates individually for each year of support requested. In the space provided on the templates, indicate the year as well as start and end dates for the proposed budget period. (Be sure the amounts entered in the Budget Detail(s) match the amounts in the online budget summary in Section #7).

- **<u>Budget Detail – Direct Costs</u>**

  Personnel - List the names and positions of all professional and non-professional personnel involved in the project, whether or not salaries are requested. Indicate the percent effort on the project for all personnel. For each individual, be sure to complete all fields on the Budget Detail in full on the template provided. In accordance with National Institutes of Health (NIH) policy, the institutional base salary of an individual may not exceed the current federal salary cap of $187,000. 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.

  Equipment - List all items of equipment greater than $5,000 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.

  Supplies - Itemize supplies such as glassware, chemicals, animals, etc., 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.

Travel - Describe the purpose of CF-relevant travel. Up to **$1,250 per person, per year, may be requested.** Please note: Expenses for travel outside the North American continent, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable without prior written approval from the CFF Grants and Contracts Office. Registration fees associated with conferences should be listed under "Other Expenses."

Patient Costs - Funds may be requested for patient costs specifically related to the proposed QI project. The basis for estimating funds requested in this category must be justified and provide detailed information regarding the proposed costs (e.g., number of procedures, cost per procedure, ancillary costs). The scientific need for patient costs will be considered in the review. Please note that participant reimbursement and compensation should be listed in "Other Expenses"; and consulting physician charges for project-related services should be listed under "Consultant Costs." Negotiation of these costs are between the applicant institution and the service provider.

If approved as part of the application, patient 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 evaluations performed under an approved award and not a sponsor.

Other Expenses - Itemize other expenses by major categories, such as duplication costs, publication costs, conference registration fees, computer charges, etc. Justify all items.

Subcontracts* - The total cost of each subcontract (directs plus indirects) should be listed under "Other Expenses" and included in the applicant's direct costs. Detailed budgets for each subcontract must be provided for each year of support (complete and upload a Budget Detail and Budget Justification template for each subcontract for each year of support requested). Negotiations of subcontracts are between the applicant institution and the subcontractor.

- **<u>Budget Detail – Indirect Costs</u>**
  Indirect costs of up to eight percent (8%) 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
  - Tuition

***For applications that include a subcontract with a third party, the applicant may request indirects only on the first $25,000 of each subcontract per project period.**

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

D. QUALITY IMPROVEMENT PROJECT PLAN (template available online)

- Key figures and legends must be included in the QI Project Plan. If uploaded as Appendices, they will NOT be reviewed.
- Type the PI's name in the space available in the header of the template. The template will track page numbers at the bottom.
- *Page limit:* 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.
- If your application is a resubmission of an earlier application, revisions should be clearly indicated by a change in font, bolded or underlined. CFF will not review resubmissions that have not been revised.

a. **Hypothesis and Specific Aims**: State concisely and realistically the intent of the proposed QI project and the hypothesis to be tested. The specific aims should be relevant to the mission of the Cystic Fibrosis Foundation. Do not exceed one page.
b. **Background and Significance**: Briefly describe the background. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this QI project by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF in particular those listed as areas of special interest to CFF. In addition, describe the relationship of the proposed work to your long-term career goals. Preference will be given to applicants who express an interest in a long-term career in CF-related work and research. Do not exceed three pages.
c. **Preliminary Results**: If applicable, provide a detailed discussion of any preliminary results.
d. **Quality Improvement Project Design and Methods**: Provide a detailed discussion of the QI project design and procedures to be used to accomplish specific aims. Please discuss: study hypothesis; primary and secondary outcome measures; study design; details of the intervention, timeline, a description of your proposed data analysis and statistical procedures. Although no page limit is specified for this section, make every attempt to be concise and succinct. Discuss the potential limitations as appropriate and alternative strategies for achieving the aims.

e. **Consultant Arrangements**: If the proposed project includes consultant arrangements and/or collaboration with other individuals outside the applicant's group, describe the working relationships and support this description by letter(s) of intent signed by collaborating individual(s). If clinical material required by this project 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.

f. **Literature Cited**: References should be numbered in the sequence that they appear in the text and listed at the end of the QI 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).

E. FACILITIES AVAILABLE (template available online)

Describe the facilities and equipment available at the applicant's institution that will be used for this project, such as laboratory, clinical, animal, computer, office, etc. Provide any additional information about the environment, including any support services available that will be utilized. Describe their pertinent capabilities, proximity and anticipated extent of use. If facilities or equipment at a consultant's or collaborative site will be used, they should be identified and clearly described. There is no page limit. Use continuation pages, if necessary.

F. VERIFICATION OF APPLICANT INSTITUTION'S TAX STATUS (upload as PDF documents)

The CFF Grants and Contracts Office must have a copy of the applicant institution's current W9 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 documentation verifying the organization's Federal tax status. Awards are not issued prior to having these documents on file with the CFF Grants and Contracts Office.

G. ORGANIZATION ASSURANCES & CERTIFICATIONS (if applicable and available, upload as PDF documents as Appendices)

CFF requires, as applicable, all necessary Institutional Review Board (IRB) approvals for human subject research, Institutional Animal Care and Use Committee (IACUC) approval for animal research, and Institutional Biosafety Committee (IBC) approval for recombinant DNA research. Copies of these approvals, if available at the time the application is submitted, must be uploaded with the application as appendices, or provided to CFF as soon as they are available. Delays in providing these approvals to CFF will affect the release of payments to Awardees. Please note, in the event the IRB has determined a study is exempt, documentation demonstrating the exempt status must be submitted to CFF.

H. APPENDICES (template available online, upload documents as PDF files)

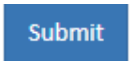
Appendices are restricted to the following three (3) categories:

- Up to three (3) reprints of the applicant's work relating to the general area of work in the proposal.
- Letters of support, collaboration, and/or reference:
  - **a.** If the applicant is not a CF Center Director or Co-Director, a letter of support from the Center Director is required.
  - **b.** If there are Co-Investigators, a letter of collaboration is required from each.
  - **c.** Letters of reference are optional but encouraged.
- Certification of IRB approval, or other applicable organization assurances documents such as IACUC and IBC Approval Letters, if available at the time of application.

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

11. **Validate:** Upon completing the application, click on the **"Validate"** button on the main screen. Attend to any omissions/errors as prompted onscreen, and then click **"Validate"** again.

12. **Print Face Pages:** Follow the prompts on the screen to generate and print a face page. The Face Page will be populated automatically with data entered in the online application (applicant's name, institution, title of application, etc.). The Face Page must be signed by the Principal Investigator and Authorized Institutional Official. **Scan and email the signed Face Page to grants@cff.org in conjunction with the application submission on proposalCENTRAL.** (In the subject line indicate "SIP 2018 Signed Face Page"). No hardcopy is required.

13. **Submit:** Click on the blue button with white lettering. 

CFF will not receive your application unless the submit button is clicked.

Confirmation: Applicants will receive an e-mail confirmation from proposalCENTRAL (not from CFF) that the application was successfully submitted. This e-mail will be your only acknowledgement. If you do not receive this confirmation, please contact proposalCENTRAL immediately to ensure that your submission was submitted and processed.

For technical support with the online application:

proposalCENTRAL at pcsupport@altum.com or

800-875-2562 on weekdays, 8:00 a.m. to 5:00 p.m. (Eastern)

For program/content information:

CFF Grants and Contracts at grants@cff.org or 301-841-2614

VI. ELECTRONIC APPLICATION CHECKLIST

Application Deadline: Monday, April 2, 2018 at 5:00 PM (ET)

Applications must be submitted at proposalCENTRAL: https://proposalcentral.altum.com/

A PDF copy of the signed Face Page should be emailed to CFF (grants@cff.org) by the application deadline. The Face Page must be signed by the Principal Investigator and Authorized Institutional Official. In the subject line indicate "SIP 2018 Signed Face Page". The complete application must be submitted online via proposalCENTRAL.

Face Page 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
  - ☐ Recombinant DNA Biosafety information
  - ☐ Research Involving Animals information

Quality Improvement Project Plan, Supporting Documents and Appendices:

- ☐ Abstracts (complete online)
- ☐ Biographical Sketches of Key Personnel - (upload)
- ☐ Other Support - (upload)
- ☐ Budget Detail for each year and subcontract, when applicable - (upload)
- ☐ Budget Justification for each year and subcontract, when applicable - (upload)
- ☐ QI Project Plan - (upload)
  - ☐ Hypothesis and Specific Aims
  - ☐ Background and Significance
  - ☐ Preliminary Results
  - ☐ Quality Improvement Project Design and Methods
  - ☐ Consultants/Collaborative Arrangements
  - ☐ Literature Cited (not included in QI Project Plan page limitation)
- ☐ Facilities Available - (upload)
- ☐ Verification of Applicant Institution's Tax Status - (upload)
  - ☐ W-9 (signed and dated within the past three years)
  - ☐ 501(c)3 or equivalent tax status letter
- ☐ Appendices (upload as PDF documents, if applicable)
  - ☐ Up to three (3) reprints of the applicant's work relating to the general area of work in the proposal
  - ☐ Letters of support, collaboration, and/or reference:
    - **a.** If the applicant is not a CF Center Director or Co-Director, a letter of support from the Center Director is required
    - **b.** If there are Co-Investigators, a letter of collaboration is required from each
    - **c.** Letters of reference are optional but encouraged
  - ☐ Certification of IRB approval, or other applicable organization assurances documents such as IACUC and IBC Approval Letters, if available at the time of application