STeP IT UP CF: Stimulating ImProved Health and Well-being in Cystic Fibrosis

Protocol V1.1, Approved 28Mar2020

With Statistical Analysis Plan

NCT04018495

MEDICAL COLLEGE OF WISCONSIN

CLINICAL STUDY PROTOCOL

STeP IT UP CF: STimulating ImProved Health and Well-being In CysTic Fibrosis Using Integration Of Fitness Technology and Port CF. A pilot in integration of wearable fitness tracker data with existing health data provided by CF foundation Patient Registry (Port CF).

Clinical Trials.gov Number: NCT #04018495

Rose Franco, M.D.

Version 1.0, April 10, 2019

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PROTOCOL SIGNATURE PAGE

Protocol No.: 1.0 **Version Date:** 10APR2019

1. I agree to follow this protocol version as approved by the MCW Institutional Review Board (IRB).
2. I will conduct the study in accordance with applicable IRB requirements, federal regulations, and state and local laws to maintain the protection of the rights and welfare of study participants.
3. I certify that I, and the study staff, have received the requisite training to conduct this research protocol.
4. I have read and understand the information in the Investigator's Brochure (or Manufacturer's Brochure) regarding the risks and potential benefits. I agree to conduct the protocol in accordance with Good Clinical Practices (ICH-GCP), the applicable ethical principles, the Statement of Investigator (Form FDA 1572) and with local regulatory requirements. In accordance with the FDA Modernization Act, I will ensure the registration of the trial on the www.clinicaltrials.gov website.
5. I agree to maintain adequate and accurate records in accordance with IRB policies, Federal, state and local laws and regulations.

MCW Principal Investigator / Study Chair

Rose Franco, MD

Printed Name

Signature Date

Title: **STeP IT UP CF: STimulating ImProved Health And Well-being In CysTic Fibrosis Using** Integration Of Fitness Technology and **Port CF. A pilot in integration of wearable fitness tracker data with existing health data provided by CF foundation Patient Registry (Port CF).**

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REVISION HISTORY

Revision history is presented in reverse order so that the information pertaining to the most current version of the protocol is presented first in this section.

Version 1.1, Version Date 21JAN2019

Clarification of exclusion criteria for equipment needed for proper use of fitness tracker

Updated study visit timelines and edited information gathered from Visit 2 and Sick visits

Version 1, Version Date 10APR2019

Initial submission of the protocol.

PROTOCOL SUMMARY

Title	**STeP IT UP CF: STimulating ImProved Health And Well-being In CysTic Fibrosis Using Integration Of Fitness Technology and Port CF. A pilot in integration of wearable fitness tracker data with existing health data provided by CF foundation Patient Registry (Port CF)**
Protocol Number	PRO00034812
Principal Investigator	Rose Franco, M.D.
Study Sites	Medical College of Wisconsin & Froedtert Hospital
Clinical Trial Phase	Pilot
Study Disease	Cystic Fibrosis
Main Eligibility Criteria	**Inclusion Criteria** 1. Adult patients at least 18 years of age 2. Current diagnosis of cystic fibrosis **Exclusion Criteria** A potential subject who meets any of the following exclusion criteria is ineligible to participate in the study. 1. Inability to commit to at least 3 months of use of the fitness tracker and routine follow up in CF clinic 2-5 months from enrollment. 2. Inability to speak and understand English 3. Those patients without dedicated access to a smartphone, or tablet with internet and blue tooth capabilities. 4. Those unwilling to sign an informed consent form
Study Rationale	Cystic fibrosis is a hereditary condition that for most leads to a significantly shortened lifespan and impaired quality of life. The CF research community has strived for new interventions to improve lung health with dramatic improvements in patient survival over the last 20 years. Fitness trackers could be helpful for those with CF through evaluating general trends in activity level, intensity of activity and sleep quality and timing. Further, integration of data from

	wearable health tracking with objective biologic/medical data would allow analysis of trends between these core components of a healthy lifestyle and medical outcomes. The objective of this pilot study is to demonstrate the feasibility of integrating the personal health tracker data with the medical data stored in CFFPR to facilitate larger multicenter interventional studies to continue improving care in this deserving population
Primary Objectives	To provide proof of concept for integrating existing medical data from CFFPR with long term monitoring of patterns in sleep and activity available through individual fitness trackers (i.e. Fitbit).
Secondary Objectives	AIM 1: Demonstrate that participants will consistently use and upload data from the fitness tracker as measured by use of at least 20 hours per day and uploading of at least 75% of activity. AIM 2: Develop integration tool for the data from the Fitbit with data from CFFPR AIM 3: Analyze the data trends from the Fitbit for activity and sleep with health trends from the CFFPR (FEV1, BMI, exacerbation rates).
Endpoints	Results of the project will allow the CF foundation to determine if integration of these databases is feasible. Ability to develop interventional studies using fitness trackers with interventions with exercise/sleep therapies
Study Design	Single-center pilot, correlational study to provide proof of concept for integrating existing medical data from CFFPR with long term monitoring of patterns in sleep and activity available through individual fitness trackers (i.e. Fitbit).
Study Agent/ Intervention Description	Fitbit tracker; is an activity tracking product that is wireless-enabled wearable technology device that measures data such as the number of steps walked, heart rate, quality of sleep, steps climbed, and other personal metrics involved in fitness
Number of Subjects	21
Duration of Follow up	3-5 Months
Estimated Time to Complete Enrollment:	12 months
Statistical Methodology:	For Aim 1 and Aim 2 we will report descriptive statistics, such as mean, median and standard deviation, for the number of days of use, days of use over 20 hours and average hours of use per day (total hours of use/total days of use) in the study. For Aim 3. We will conduct explorative data analysis to get preliminary information for designing a full-scale prospective study. First, we will report summary statistics, such as mean, median, standard deviation and quartile range, for continuous measurement and percentage for binary measurement, of heart rate, activity levels, sleep time and quality of sleep for every month and summary statistics for FEV1, BMI and CF exacerbation at enrollment and 3-month and differences between enrollment and 3-month. To identify

	what information of heart rate, activity levels, sleep time and quality of sleep is potentially associated with the differences between enrollment and 3-month in FEV1 and BMI and CF exacerbation for 3- month, we will use Pearson correlations for FEV1 and BMI and comparing means or medians of the wearable metrics between the subgroups with and without CF exacerbation in 3 months. We will also consider mean or median values of the wearable metrics measured last 3-/2-/1-month prior to the follow-up to determine the extent to how latest metrics are associated with clinical outcomes.
Efficacy Assessments	To measure the benefit of using Fitbit trackers for those with CF through evaluating general trends in activity level, intensity of activity and sleep quality and timing (Jankelowitz et al., 2005). Further, integration of data from wearable health tracking with objective biologic/medical data would allow analysis of trends between these core components of a healthy lifestyle and medical outcomes.
Unique Aspects of this Study	This pilot study is to demonstrate the feasibility of integrating the personal health tracker data with the medical data stored in CFFPR to facilitate larger multicenter interventional studies to continue improving care in this deserving population

STUDY CALENDAR

The below study chart is described in detail in Section 5 Study Procedures.

Period/ Procedure	Screening/Enrollment	2-5 monthFollow up visit	Sick Visit
Study Day/Visit Day	**1**	**2**	**3**
Eligibility Criteria	X		
Informed Consent	X		
Demographics	X		
Assessment of Adverse Events		X	X
Device Administration			
Fitbit Inspire HR provided	X		
Fitbit Training	X		
Sync Device every 5 days	X	X	X
Questionnaires			
CF QOP	X	X	X
PQSI	X	X	X
Medical history collected as standard of care			
Lung Function	X	X	X
BMI	X	X	X

Period/ Procedure	Screening/Enrollment	2-5 monthFollow up visit	Sick Visit
Study Day/Visit Day	**1**	**2**	**3**
CF exacerbation rate	X	X	X

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
CF	Cystic Fibrosis
CFFPR	Cystic Fibrosis Foundation Patient Registry
CFTR	CFTR
CRC	clinical research coordinator
DSMB	Data and Safety Monitoring Board
FEV	Forced Expiratory Volume
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IND	investigational new drug application
IRB	Institutional Review Board
PQSI	Pittsburg Quality Sleep Index
PI	Primary Investigator
QOL	Quality of Life
SD	standard deviation
UP	unanticipated problem
UPIRSO	unanticipated problems involving risks to subjects or others

1 BACKGROUND

Cystic Fibrosis

Cystic fibrosis is a hereditary condition that for most leads to a significantly shortened lifespan and impaired quality of life. The CF research community has strived for new interventions to improve lung health with dramatic improvements in patient survival over the last 20 years. Beginning with enhanced lung clearance techniques, Pulmozyme, and new antibiotics providers saw a jump in the life expectancy of CF patients between 1995 and 2010. (Keogh, Szczesniak, Taylor-Robinson, & Bilton, 2018) Previous work has resulted in a very good understanding of the genetics behind the mutations that lead to the CFTR protein alterations and the varying phenotypes of the disease. The CF foundation is now projecting a doubling of the life expectancy of CF patients in the next 10 years ("Cystic Fibrosis Trust Cystic fibrosis registry report 2017. ,"
2017;"Resources/Patient-Registry/Understanding-Changes-in-Life-Expectancy.,"2016; Stephenson et al., 2017; Sykes et al., 2016; "WHO Guidelines Approved by the Guidelines Review Committee," 2010) much of which is related to the CFTR modulator therapies current and under development. More successes over the next decade will likely move cystic fibrosis
from a disease that kills young adults to a disease that people live with into old age. Aging gracefully means clinicians must look at the totality of care for these patients and specifically at quality of life factors such as exercise, diet, and sleep patterns and the interplay these factors have on lung health, glycemic control, bone health and general wellbeing with a goal to improve all aspects of care so that the patient living with CF has the best possible quality of life.

People with chronic illness often end up with an imbalance of the core components of a balanced healthy lifestyle including adequate sleep, regular exercise and a balanced diet. Once this imbalance is present there is a much higher chance that these factors will contribute themselves to additional medical complications as well as decreased quality of life and increased mental health issues.

Physical activity is recognized by the World Health Organization as a crucial component to maintaining health and preventing disease ("WHO Guidelines Approved by the Guidelines Review Committee," 2010). Several studies have shown that physical activity is independently related to aerobic capacity in cystic fibrosis (CF) (Hebestreit et al., 2006).

The CF community has also recognized the value of regular exercise and studies have demonstrated that regular physical activity can positively impact lung function (Kriemler et al., 2013), improve general wellbeing, exercise tolerance and bone health in patients with CF (Tejero Garcia et al., 2011).

Small studies in adults with CF suggest that those with poorer lung function suffer with exacerbations more frequently than those with better lung function (Savi et al., 2015). Short-term (6-8 weeks) inpatient and outpatient rehab programs for CF patients have shown improved overall lung function and exercise capacity (Gruber, Orenstein, Braumann, Paul, & Huls, 2011; Santana Sosa et al., 2012). In addition, one small 12-month study in children suffering from CF demonstrated that exercise reduces CF exacerbation frequency (Urquhart et al., 2012). While other small and short-duration studies have demonstrated similar improvements, it is not clear that a change in one's exercise and conditioning routine can alter the frequency of exacerbations seen in adults with CF.

Decades of research has demonstrated that chronically deficient sleep (time or quality) results in higher risk for poor health: everything from mental health issues to accidents to excess risk for obesity and cardiovascular disease and even premature death. ("Centers for Disease Control and Prevention. Insufficient sleep is a public health problem.,"; Luyster, Strollo, Zee, & Walsh, 2012; Van Dongen, Maislin, Mullington, & Dinges, 2003; "WHO-Europe Bonn Germany, January 22-24, 2004 (Role of Sleep in health)," 2004) There are limited studies of sleep and disorders of sleep in CF. Generally, the findings point to poorer quality (decreased deep sleep, increased awakenings, increased daytime sleepiness) (Amin, Bean, Burklow, & Jeffries, 2005; Dancey, Tullis, Heslegrave, Thornley, & Hanly, 2002; Milross et al., 2002; Vandeleur et al., 2017). The reason for this poor sleep is only partly explained by CF exacerbation or declining lung function. Defective expression of CFTR (expand CFTR) gene in

certain areas of brain (specifically the retina and anterior hypothalamus) could contribute to both changes in the timing of sleep and the quality of sleep (Jensen et al., 2017). The role of sleep alterations in glucose metabolism has been studied (Gonzalez-Ortiz, Martinez-Abundis, Balcazar-Munoz, & Pascoe-Gonzalez, 2000; Punjabi et al., 2002). but no clinical study of CF Related Diabetes and sleep patterns or exercise patterns has been completed (Hardin, Leblanc, Marshall, & Seilheimer, 2001).

The newest personal fitness monitors allow for both short term and long-term trending in activity and sleep and are both affordable and easy to operate. Data generated by this technology afford the possibility of better understanding one's personal state of general wellness from how much activity to the level of intensity to the quality and quantity of sleep one is getting. The role of an activity monitor in improving activity and fitness has been studied and may have the most impact
on those with lowest activity levels in some populations (Beattie et al., 2017; Schrager et al., 2017). Regarding sleep tracking, the validity of sleep tracking programs has also been assessed and total sleep time and sleep quality can be measured with fair accuracy (de Zambotti, Baker, & Colrain, 2015; Meltzer, Hiruma, Avis, Montgomery-Downs, & Valentin, 2015).

Fitness trackers could be helpful for those with CF through evaluating general trends in activity level, intensity of activity and sleep quality and timing (Jankelowitz et al., 2005). Further, integration of data from wearable health tracking with objective biologic/medical data would allow analysis of trends between these core components of a healthy lifestyle and medical outcomes.

The CF community has been collecting biologic/medical data on patients now for over 30 years through the CF Foundation Patient Registry (CFFPR). This provides individual as well as center specific trends through tracking weight/BMI, lung function, frequency of exacerbations as well lab and test results such as glycemic control and bone density results. This data has assisted CF centers in improvements in care delivery (Warwick, 2001) through quality improvement (Johnson,
Butler, Konstan, Morgan, & Wohl, 2003) and best practice sharing between centers (Schechter, Fink, Homa, & Goss, 2014). In 2017 all centers have now risen to near real-time reporting of lung function, exacerbation rates, weight and diabetes control trends for patients to encourage conversations and real behavior change around medical adherence.

The objective of this pilot study is to demonstrate the feasibility of integrating the personal health tracker data with the medical data stored in CFFPR to facilitate larger multicenter interventional studies to continue improving care in this deserving population.

Methods

Potential subjects will be identified during regular team meetings held by a dedicated care team for CF patients that includes members of the study staff. Patients who are identified as potential participants will be contacted by a trained member of the study team to discuss participation. The study team will work with patients to arrange for signing of an informed consent form at their next scheduled clinic appointment.

All subjects will be consented to participate in this observational study for a minimum 3 months to accommodate their clinic schedule. There will be a minimum of 2 clinical visits after enrollment (clinical visit 1 at set up and 2-5 months follow up) as well as any sick visits. This visit schedule was selected to coincide with current care schedules.

At the initial visit all consented subjects will be provided a Fitbit Inspire HR and shown the proper use and care of the tracker. The research coordinator will confirm the subject's ability to upload data from the device to their study Fitbit account (deidentified) under direct observation. The subjects will also receive instruction in how to document their activity and sleep in the diary app associated with their Fitbit. (The subjects will have access to instructional videos and help desk
through the Fitbit resource center as well). The research coordinator will monitor the study specific FitaBase for the duration of the study (once a week for 3 months) and contact the patient via their preferred method of contact with encouragement to consistently upload data if needed.

During the initial visit and any follow up clinic visits subjects will complete a general quality of life in CF survey-CF QOL and a sleep quality index-Pittsburgh Sleep Quality Index (PQSI) through Redcap to assist in a comprehensive integration of data.

This study will quantify the activity and sleep patterns of the CF patients through use of the provided fitness monitor (Fitbit- Inspire HR) that measures heart rate, activity level (number of steps, intensity of exercise (moderate to intense based on HR vs movement on GPS-Fitbit analytics), sleep time and quality of sleep over 3 months. To provide the most accurate data from the device subjects will need to sync their device at least every 5 days to keep the 5-minute and 1-minute data for the prior days of use. The process of synchronization/downloading is nearly effortless for those with a smart phone or computer as every time the device is near these devices it should download the data collected. In addition, the Fitbit app and website has additional programs including a diary where subjects can document their exercise, activity and even sleep habits. Whenever possible the subject will document their activity through this app to provide validation of the data collected by the sensors.

The FitaBase has preset analysis functions to allow for data report at daily, weekly, monthly intervals. The is a deidentified database and subjects will be given assigned subject codes for this database to prevent sharing of identifiable information. To further secure patient privacy, all subjects will have a study email account set up to tie to the trackers during the study.

Quality control for Fitbit data will include confirming Fitbit uploads weekly (remote access) and comparison of this data against the patient activity/sleep diary entry for accuracy at the time of the phone conversation at 1 week and 1 month and all clinical visits (sick visit/s, Month 3).

At each CF clinical visit (initial visit, routine scheduled checkup, and any sick visits/hospitalization) the research team will check in with the subjects and confirm there are no issues or concerns with the device and/or address study compliance issues.

If a Fitbit stops working, the Fitbit program will be notified by the research coordinator and a new device sent to the research site to be dispensed by the research coordinator to the subject (via mail or in person) after confirming it is tied to the subject number's appropriate account in FitaBase. Additional devices will be available to the research site to dispense in the event of a lost device (not supported by the Fitbit care program).
Clinical care visits and hospitalizations during the trial period of three months will be entered into the CFFPR national database (standard practice). Data of specific interest include: lung function (FEV1), BMI, and CF exacerbation rates. The exacerbation will be defined by the treating CF provider (generally this is reported as part of each visit (key features of a CF exacerbation include all the following but does not require any more than 3 of the following: Weight loss (>2 lbs.),
increased cough/increased sputum production, disturbed sleep due to coughing, increased fatigue/inability to do daily activities due to breathing problems/fatigue, fevers, fall in FEV1 by 5% or more)).

Any technical questions from the patient regarding the data collected by the fitness tracker will be answered by the research
coordinator.

2 HYPOTHESIS AND OBJECTIVES

This pilot, single center, correlational study will provide proof of concept for integrating existing medical data from CFFPR with long term monitoring of patterns in sleep and activity available through individual fitness trackers (i.e. Fitbit).

The data collected for each subject from the personal fitness monitors will be trended with daily, weekly and monthly averages over 3 months (activity level, time and intensity of exercise, sleep total time and quality

(percentage deep sleep). This information will be coupled with the CFFPR data health parameters as reported with every clinic visit and any hospitalizations for each subject.

2.1 Aims

AIM 1: Demonstrate that participants will consistently use and upload data from the fitness tracker as measured by use of at least 20 hours per day and uploading of at least 75% of activity.

AIM 2: Develop integration tool for the data from the Fitbit with data from CFFPR.

AIM 3: Analyze the data trends from the Fitbit for activity and sleep with health trends from the CFFPR (FEV1, BMI, exacerbation rates).

3 STUDY DESIGN

3.1 General Description

The study center has identified 147 adult patients ranging from 18 to 69 years of age with CF. For this feasibility study a total of 21 patients will be enrolled and while we will not assign patients to cohorts or limit enrollment based on lung function at the end of the study, we will stratify enrolled patients to explore trends. The cohorts will be constructed ad hoc to facilitate an accurate and clinically meaningful analysis. This will allow for trend analysis to see if more advanced disease is a factor in adherence to use of the Fitbit and an exercise regimen.

The study will be carried out by a dedicated research group consisting of seven full time research coordinators, a research assistant, and a part-time systems specialist within the PI's Division that has conducted numerous trials and continues to support a robust and successful CF research program. The study will be assigned at minimum two research coordinators to provide every eligible patient the opportunity to participate. The study research coordinator group has previous experience with fitness tracker software and management of deidentified database related to a fitness tracker used in a large multicenter clinical trial.

Number of Subjects

Up to 21 patients may be consented into this trial. Twenty-one patients are needed to meet the aims of this trial.

3.1.1 Primary Endpoint(s)

For Aim 1 and Aim 2 we will report descriptive statistics, such as mean, median and standard deviation, for the number of days of use, days of use over 20 hours and average hours of use per day (total hours of use/total days of use) in the study. Secondary Endpoint(s)

For Aim 3. We will conduct explorative data analysis to get preliminary information for designing a full-scale prospective study. First, we will report summary statistics, such as mean, median, standard deviation and quartile range, for continuous measurement and percentage for binary measurement, of heart rate, activity levels, sleep time and quality of sleep for every month and summary statistics for FEV1, BMI and CF exacerbation at enrollment and follow-up visit and differences between enrollment and follow-up visit. To identify what information of heart rate, activity levels, sleep time and quality of sleep is potentially associated with the differences between enrollment and follow-up visit in FEV1 and BMI and CF exacerbation, we will use Pearson correlations for FEV1 and BMI and comparing means or medians of the wearable metrics between the subgroups with and without CF exacerbation in 3 months. We will also consider mean or median values of the wearable metrics measured last 3-/2-/1-month prior to the follow-up to determine the extent to how latest metrics are associated with clinical outcomes.

3.2 Study Timeline

See Study Calendar.

4 PATIENT SELECTION

4.1 Eligibility Criteria

Adults with Cystic Fibrosis

4.2 Inclusion Criteria

Age >18, Cystic Fibrosis

4.3 Exclusion Criteria

A potential subject who meets any of the following exclusion criteria is ineligible to participate in the study.

Those unable to commit to at least 3 months of participation with the fitness tracker and return for a routine follow up visit from time of enrollment at study CF
center. Inability to speak and understand English. Those patients without dedicated access to a smartphone, tablet, or computer with internet for syncing device and completing patient diary.
Those patients unwilling to sign an informed consent form.

5 STUDY ENTRY AND WITHDRAWAL; STUDY PROCEDURES

5.1 Study Entry Procedures

5.1.1 Required Screening

The study-specific assessments are detailed in this section and outlined in the Study Calendar.

When a CF patient 18 years of age or older is identified the study staff will review the inclusion/exclusion against the IRB approved criteria to ensure eligibility. If appropriate, they will pursue an informed consent discussion with the patient. All patients reviewed will be documented in a screening log and reason for exclusion for reporting purposes.

A signed ICF copy will be given to the subject and a copy will be filed in the medical record. The original will be kept on file with the study records.

All patients who are consented will be registered and randomized in OnCore®, the MCW Clinical Trial Management System. The system is password protected and meets HIPAA requirements.

Screening Assessments

- Confirmation of Eligibility Criteria listed in Section 4.2 and 4.3
- Signed written informed consent form by the patient

5.1.2 Study Procedures, Day 1

- all consented subjects will be provided a Fitbit Inspire HR and shown the proper use and care of the tracker. The research coordinator will confirm the subject's ability to upload data from the device to their

study Fitbit account (deidentified) under direct observation. The subjects will also receive instruction in how to document their activity and sleep in the diary app associated with their Fitbit. All subjects will have access to instructional videos and a help desk through the Fitbit resource center as well. The research coordinator will monitor the study database for the duration of the study and contact the patient via their preferred method of contact with encouragement to consistently upload data if needed. Collection of demographic information

5.1.3 Study Procedures During Visit 1 and Visit 2

- During Visit 1 and Visit 2, subjects will complete a general quality of life in CF survey (CFQ-R) and a sleep quality index-Pittsburgh Sleep Quality Index (PQSI) survey.

To provide up to date and accurate data from the device, subjects will need to sync their device at least every 5 days to store their activity information appropriately into the study database. In addition, the Fitbit app and website have additional programs including a diary where subjects can document their exercise, activity and even sleep habits. Whenever possible the subject will document their activity through this app to provide validation of the data collected by the sensors.

The study coordinator will confirm Fitbit uploads with the subject by comparison of the data entered in the patient activity/sleep diary entry to the data from the Fitbit during the phone call visits with the subject.

A database used for collecting the Fitbit data will only be given assigned subject codes to prevent sharing of identifiable subject information. To further secure patient privacy, all subjects will have a study email account set up to tie to the trackers during the study.

If the Fitbit stops working, the subject should contact the study coordinator to arrange for a replacement Fitbit. Fitbits that are lost will not be replaced.

5.2 Study Withdrawal Procedures

5.2.1 Duration of Therapy: A patient may remain in the study up to 3-months.

5.2.2 Patient-Initiated Withdrawal: A patient may decide to withdraw from the study at any time.

5.2.3 Investigator-Initiated Withdrawal: The Investigator will withdraw a patient whenever continued participation is no longer in the patient's best interests. Reasons for withdrawing a patient include, but are not limited to, disease progression, the occurrence of an adverse event or a concurrent illness, a patient's request to end participation, a patient's noncompliance or simply significant uncertainty on the part of the Investigator that continued participation is prudent.

5.2.4 Withdrawal Documentation Procedure: The reason for study withdrawal and the date the patient was removed from the study must be documented in OnCore.

6 TREATMENT PLAN

6.1 Standard of Care Procedures

6.2 Follow-Up Period

Patients will be followed for 90 days after enrollment or until death, whichever occurs first.

7 ADVERSE EVENTS: DEFINITIONS AND REPORTING REQUIREMENTS

7.1 Definitions

7.1.1 Adverse Event (AE) and Serious Adverse Events (SAE)

Patients enrolling in this trial are not expected to have any adverse events related to the study. Should an event occur the investigator and his or her team will follow the Medical College of Wisconsin policies related to adverse event reporting. This information may be found on the Human Research Protection Program website.

Serious AE (SAE) means any untoward medical occurrence related to study specific procedures/interventions:

- **Death.** Results in death.
- **Life threatening**. Is life threatening (refers to an AE in which the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe).
- **Hospitalization**. Requires inpatient hospitalization or prolongation of an existing hospitalization (see clarification in the paragraph below on planned hospitalizations).
- **Disability/incapacity**. Results in persistent or significant disability or incapacity. (Disability is defined as a substantial disruption of a person's ability to conduct normal life functions).
- **Medically important event**. This refers to an AE that may not result in death, be immediately life threatening, or require hospitalization, but may be considered serious when, based on appropriate medical judgment, may jeopardize the patient, require medical or surgical intervention to prevent 1 of the outcomes listed above, or involves suspected transmission via a medicinal product of an infectious agent. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse; any organism, virus, or infectious particle (e.g., prion protein transmitting Transmissible Spongiform Encephalopathy), pathogenic or nonpathogenic, is considered an infectious agent.

Clarification should be made between a serious AE (SAE) and an AE that is considered severe in intensity (Grade 3 or 4), because the terms serious and severe are NOT synonymous. The general term severe is often used to describe the intensity (severity) of a specific event; the event itself, however, may be of relatively minor medical significance (such as a Grade 3 headache). This is NOT the same as serious, which is based on patient/event outcome or action criteria described above and is usually associated with events that pose a threat to a patient's life or ability to function. A severe AE (Grade 3 or 4) does not necessarily need to be considered serious. For example, a white blood cell counts of 1000/mm3 to less than 2000 is considered Grade 3 (severe) but may not be considered serious. Seriousness (not intensity) serves as a guide for defining regulatory reporting obligations.

7.1.2 Unanticipated Problem Involving Risk to Subject or Other (UPIRSO)

The investigator and his or her team will follow the Medical College of Wisconsin policies related to unanticipated problems involving risks to subjects or others. This information may be found on the Human Research Protection Program website.

7.1.3 AE Attribution and Grading

Adverse Event Grading

Grade	Description
0	No AE (or within normal limits).
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
2	Moderate; minimal, local or noninvasive intervention (e.g., packing cautery) indicated; limiting age-appropriate instrumental activities of daily living (ADL).
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.
4	Life-threatening consequences; urgent intervention indicated.
5	Death related to AE

Adverse Event Attribution

Attribution is an assessment of the relationship between the AE and the medical intervention.

Relationship	Attribution	Description
Unrelated to investigational agent/intervention	Unrelated	The AE *is clearly **NOT** related* to the intervention
	Unlikely	The AE *is **doubtfully related*** to the intervention
Related to investigational agent/intervention	Possible	The AE ***may be related*** to the intervention
	Probable	The AE ***is likely related*** to the intervention
	Definite	The AE ***is clearly related*** to the intervention

Relationship Assessment: In-Depth Definitions

For all collected AEs, the clinician who examines and evaluates the subject will determine the adverse event's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below:

Definitely Related: There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to drug administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.

Probably Related: There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time sequence to administration of the drug, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.

Possibly Related: There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g., the subject's clinical condition, other concomitant events). Although an adverse drug event may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.

Unlikely: A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the trial medication) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the subject's clinical condition, other concomitant treatments).

Unrelated: The AE is completely independent of study drug administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

7.2 Most Monitoring and Recording an Adverse Event

Definition. Any clinically relevant deterioration in laboratory assessments or other clinical finding is considered an AE.

Reporting source. AEs may be spontaneously reported by the patient and/or in response to an open question from study personnel or revealed by observation, physical examination or other diagnostic procedures.

Prior to the trial. Planned hospital admissions or surgical procedures for an illness or disease that existed before the patient was enrolled in the trial are not to be considered AEs unless the condition deteriorated in an unexpected manner during the trial (e.g., surgery was performed earlier or later than planned).

Pretreatment events following signed informed consent. For serious pretreatment events, the investigator must determine both the intensity of the event and the relationship of the event to study procedures.

Treatment events. For serious AEs, the investigator must determine both the intensity of the event and the relationship of the event to study drug administration.

Not serious AEs. For non-serious AEs, the investigator must determine both the intensity of the event and the relationship of the event to study drug administration.

Follow-up of Adverse Events

All adverse events will be followed with appropriate medical management 30 days following the last dose of the study drug or treatment or until they are resolved, if they are related to the study treatment.

7.2.1 Subject Complaints

If a complaint is received by anyone on the study staff, it will be discussed with the study staff and will be addressed on a case-by-case basis. The PI will be notified of any complaints. Complaints will be reported to the IRB if indicated.

If the subject has questions about his or her rights as a study subject, wants to report any problems or complaints, obtain information about the study or offer input, the subject can call the Medical College of

Wisconsin/Froedtert Hospital research subject advocate at 414-955-8844. This information is provided to the subject in their consent.

A product complaint is a verbal, written or electronic expression that implies dissatisfaction regarding the identity, strength, purity, quality or stability of a drug product. Individuals who identify a potential product complaint situation should immediately contact the sponsor and report the event. Whenever possible, the associated product should be maintained in accordance with the label instructions pending further guidance from a sponsor representative. Product complaints in and of themselves are not Reportable Events. If a product complaint results in an SAE, an SAE form should be completed.

7.2.2 Routine Reporting Procedures for AEs

Expedited Reporting Procedures for SAEs, SARs, UPIRSOs and DLTs.

Since this is an investigator-initiated study, the principal investigator, also referred to as the sponsor-investigator, is responsible for reporting serious adverse events (SAEs) to any regulatory agency and to the sponsor- investigator's IRB. All applicable SAEs must be reported to the DSMB as soon as possible, but no later than five calendar days of the sponsor-investigator's observation or awareness of the event.

Signs or symptoms reported as adverse events will be graded and recorded by the investigator, according to the CTCAE. When possible, signs and symptoms indicating a common underlying pathology should be noted as one comprehensive event.

The investigator will assess all adverse events and determine reporting requirements to the Data and Safety Monitoring Board (DSMB) and MCW's Institutional Review Board, and, when the study is conducted under an Investigational New Drug Application (IND), to the Food and Drug Administration (FDA), if it meets the FDA reporting criteria. The investigator will report SAEs to any regulatory agency and to the sponsor- investigator's IRB.

Reporting to MCW Committee Institutional Review Board

The principal investigator must report events to the MCW IRB within five business days of his/her awareness of the event.

8 PHARMACEUTICAL INFORMATION

9 STATISTICAL CONSIDERATIONS

9.1 Study Design

This is a single site, prospective, pilot study.

9.2 Sample Size and Power Estimate

With sample size 21, we can obtain the following precision: two-sided 95% confidence intervals with a width equal to 0.856 and 0.193 when the estimate of Pearson's correlation between each wearable metric and a clinical outcome is 0.1 and 0.9, respectively (Bonnett, 2000). Regarding mean differences between the subgroup with and without CF exacerbation, we do not know CF exacerbation rate, so consider two scenarios: equal group size (10/group) and 2:1 ratio (7 and 14 group sizes). The two scenarios produce two-sided 95% confidence intervals with a distance from the difference in means to the limits that are equal to 0.940 for the equal size and 0.969(Ostler, 1988) for the latter when the both estimated standard deviations are 1 (we can standardize the wearable metrics and clinical outcomes by dividing raw values by the estimated standard deviation).

9.3 Replacement Policy

Patients will only be replaced if they were consented into the trial but failed to receive study Fitbit for any reason. Patients who began the study but were unable to complete the device downloads will be included in the analysis with intent to participate.

9.4 Interim Analyses and Stopping Rules

No interim analysis is planned at this time.

9.5 Analyses Plans

Statistical support will be provided by MCW Department of Medicine Biostatistical team.

9.6 Study Team

The study team minimally consists of the principal investigator, the clinical research coordinator, and the study biostatistician. The principal investigator will meet regularly with the research coordinator and the study biostatistician to review study status. This review will include but not be limited to reportable SAEs and UPIRSOs and an update of the ongoing study summary that describes study progress in terms of the study schema. The appropriateness of further subject enrollment and the specific intervention for a next subject enrollment is addressed.

9.7 Quality Assurance

The MCW Office of Research provides ongoing quality assurance audits when requested.

9.8 Ethical Standard

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki as stated in 21 CFR §312.120(c)(4); consistent with GCP and all applicable regulatory requirements.

9.9 Regulatory Compliance

This study will be conducted in compliance with:

- The protocol
- Federal regulations, as applicable, including: 21 CFR 50 (Protection of Human Subjects/Informed Consent); 21 CFR 56 (Institutional Review Boards) and §312 (Investigational New Drug Application; and 45 CFR 46 Subparts A (Common Rule), B (Pregnant Women, Human Fetuses and Neonates), C (Prisoners), and D (Children), GCP/ICH guidelines, and all applicable regulatory requirements. The IRB must comply with the regulations in 21 CFR §56 and applicable regulatory requirements.

9.10 Pre-study Documentation

Prior to implementing this protocol at MCW, the protocol, informed consent form, HIPAA authorization and any other information pertaining to participants must be approved by the MCW IRB.

The clinical investigation will not begin until either FDA has determined that the study under the Investigational Drug Application (IND) is allowed to proceed or the Investigator has received a letter from FDA stating that the study is exempt from IND requirements.

9.11 Institutional Review Board

The protocol, the proposed informed consent form and all forms of participant information related to the study (e.g. advertisements used to recruit participants) will be reviewed and approved by the MCW Institutional Review Board. The initial protocol and all protocol amendments must be approved by the IRB prior to implementation.

Informed Consent Process

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of this therapy will be provided to the subjects and their families. Consent forms describing in detail the study interventions/products, study procedures, and risks are given to the subject and written documentation of informed consent is required prior to starting intervention/administering study product.

Potential subjects will be told, and a statement will be included that this study is designed to determine both safety and effectiveness. The consent forms will include the approved MCW IRB template language.

Consent forms will be IRB-approved and the subject (and Legally Authorized Representative, if necessary) will be asked to review the document. Upon reviewing the document, the investigator will explain the research study to the subject and answer any questions that may arise. In accordance with 46 CR 46.111, the subject will sign and date the informed consent document prior to any procedures being done specifically for the study.

A witness should only sign when required, per FH/MCW IRB policy. If a witness signs the document when not required, the study staff should document in the legal medical record (or note to file) the relationship to the patient and why a witness signed. (i.e., "Although not required, the subject's spouse was present during the consenting process and signed as the witness." Or "Although not required, hospital staff was present for consenting process and signed as a witness.")

The subjects (or their LAR) will have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The subjects may withdraw consent at any time throughout the course of the trial.

A copy of the informed consent document will be given to the subjects (or their LAR) for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely impacted if they decline to participate in this study. Study subjects will not be reconsented for continuing reviews.

After the subject's visit in which the consent is signed, it is documented in the medical chart that the consent has been signed and that all questions have been answered to the subject's satisfaction after adequate time for review of the consent. It is also documented that a copy of the consent is given to the subject. The original consent is kept with the subject's study file, and a copy of the consent is sent to the OCRICC office, which will then submit to HIM a copy of the signed consent to be scanned into EPIC, the legal medical record.

9.12 Subject Confidentiality and Access to Source Documents/Data

Subject confidentiality is strictly held in trust by the sponsor-investigator, participating investigators, and any staff. This confidentiality includes the clinical information relating to participating subjects.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the principal investigator.

The conditions for maintaining confidentiality of the subjects' records are required for the life of the data. These rules apply equally to any and all MCW projects.

One risk of taking part in a research study is that more people will handle the personal health information collected for this study. The study team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass the subject or affect his/her ability to get insurance.

While data are being collected and after all data have been collected but are still in the process of being analyzed, the subject's data/PHI are stored in the locked Clinical Research offices in the PI's Division. Databases in which the study subject information is stored and accessed are password protected, allowing for limited access by authorized personnel only. Data/PHI kept in the Case Report Forms contain the study identifiers, subject initials, date of birth and date of service.

Personal identifiers, such as name and medical record number, will be removed from accompanying lab reports and test results. Any data/PHI that are not stored for the purposes of the study are shredded.

After all study queries and analyses are completed, the data/PHI will not be destroyed but will be archived in a secure long-term storage site in order to keep an accurate record of screened and enrolled subjects for the sponsor and potential audit purposes only specific for this study. Data/PHI would not be destroyed until permission is granted by the sponsor to destroy the records.

The principal investigator will allow access to all source data and documents for the purposes of monitoring, audits, IRB review, and regulatory inspections.

The study monitor or other authorized representatives of the investigator may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. The clinical study site will permit access to such records.

9.13 Protection of Human Subjects

9.13.1 Protection from Unnecessary Harm

Each clinical site is responsible for protecting all subjects involved in human experimentation. This is

accomplished through the IRB mechanism and the informed consent process. The IRB reviews all proposed studies involving human experimentation and ensures that the subject's rights and welfare are protected and that the potential benefits and/or the importance of the knowledge to be gained outweigh the risks to the individual. The IRB also reviews the informed consent document associated with each study in order to ensure that the consent document accurately and clearly communicates the nature of the research to be done and its associated risks and benefits.

9.13.2 Protection of Privacy

As noted, patients will be informed of the extent to which their confidential health information generated from this study may be used for research purposes. Following this discussion, they will be asked to sign informed consent documents. The original signed document will become part of the patient's medical records, and each patient will receive a copy of the signed document.

9.14 Changes in the Protocol

Once the protocol has been approved by the MCW IRB, any changes to the protocol must be documented in the form of an amendment. The amendment must be signed by the investigator and approved by IRB prior to implementation.

If it becomes necessary to alter the protocol to eliminate an immediate hazard to patients, an amendment may be implemented prior to IRB approval. In this circumstance, however, the Investigator must then notify the IRB in writing within five working days after implementation.

The IRB may provide, if applicable regulatory authority(ies) permit, expedited review and approval/favorable opinion for minor change(s) in ongoing studies that have the approval /favorable opinion of the IRB. The investigator will submit all protocol modifications to the sponsor and the regulatory authority(ies) in accordance with the governing regulations.

Any departures from the protocol must be fully documented in the source documents.

9.15 Investigator Compliance

The investigator will conduct the study in compliance with the protocol given approval/favorable opinion by the IRB and the appropriate regulatory authority(ies).

Onsite Audits

Auditing is essential to ensure that research conducted at the Medical College of Wisconsin (MCW) is of the highest quality and meets MCW and regulatory agency standards.

Regulatory authorities, the IRB and/or sponsor may request access to all source documents, data capture records and other study documentation for on-site audit or inspection. Direct access to these documents must be guaranteed by the investigator, who must provide support at all times for these activities.

10 DATA HANDLING AND RECORD KEEPING

All subjects enrolled into the trial will be assigned a unique study ID number in order to maintain patient privacy and confidentiality. All data collected for the purpose of research will be entered in a secure electronic data capture system on secured servers. Information recorded for research purposes will be captured directly from the patient's electronic medical record or recorded on CRFs (or eCRFs). The patient's medical record, study CRFs, and any notes or print outs made by the study staff will be considered source documents and will be made available for inspection or review in the event of an inspection or audit by a regulatory official. All images that require Principal Investigator review will be sent de-identified using the provided de-identifying software.

All study staff will undergo appropriate training to ensure accuracy in data capture. The Principal Investigator remains responsible for the accuracy and integrity of the data collected under his or her supervision.

All study records will be retained for a minimum of 10 years per MCW policy or until two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region.

10.1 Overview

Every effort is made to uphold the integrity of the project, the research, the institution, and the researchers involved. Data collection guidelines and methodologies are carefully developed before the research begins. Investigators focus on the following to ensure data integrity: well-trained data collectors/recorders to ensure consistency and quality, well-designed data collection protocols and ongoing monitoring. In this way, study rigor and validity are maintained. Data is protected from physical damage as well as from tampering, loss or theft. This project's data management is a multidisciplinary activity that includes investigators, research coordinators and nurses, data mangers, support personnel, biostatisticians and database programmers. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

10.2 Data Management Responsibilities

10.2.1 Principal Investigator
The principal investigator oversees the management of patient records/case report forms and ensures that a) complete and accurate data will be obtained; b) patient records are maintained to include history, prescribed medication and investigational product(s), measurements, exams, evaluations and adverse events; c) corrections are applied to clinical research data according to principles of good research practice (i.e., single-line delete, date and initial). He or she will ensure that there is correlation between the case report forms and the source documents.

10.2.2 Research Coordinator
A research coordinator creates, collects and organizes clinical trial documentation. He or she ensures that source documentation and data abstraction and entry are being done at protocol specified time points.

10.2.3 Biostatistician
The biostatistician may assist in CRF development (content and design), dataset specifications (annotation of CRFs and record layout) and validation.

10.3 Handling and Documentation of Clinical Supplies

The MCW Principal Investigator will maintain complete records showing the receipt, dispensation, return, or other disposition of all investigational product. The date, quantity and batch or code number of the product, and the identification of patients to whom study product has been dispensed by patient number and initials will be included. The sponsor-investigator will maintain written records of any disposition of the study product.

The principal investigator shall not make the investigational product available to any individuals other than to qualified study patients. Furthermore, the principal investigator will not allow the investigational product to be used in any manner other than that specified in this protocol.

10.4 Source Documents

Source documents for clinical information (patient history, diagnosis, clinical and diagnostic test reports, etc.) are maintained in the patient's clinical file.

All source documents will be written following ALCOA standards:

ALCOA Attribute	Definition
Attributable	Clear who has documented the data.
Legible	Readable and signatures identifiable.
Contemporaneous	Documented in the correct time frame along with the flow of events. If a clinical observation cannot be entered when made, chronology should be recorded. Acceptable amount of delay should be defined and justified.
Original	Original, if not original should be exact copy; the first record made by the appropriate person. The investigator should have the original source document.
Accurate	Accurate, consistent and real representation of facts.
Enduring	Long-lasting and durable.
Available and accessible	Easily available for review by treating physicians and during audits/inspections. The documents should be retrievable in reasonable time.
Complete	Complete until that point in time.
Consistent	Demonstrate the required attributes consistently.
Credible	Based on real and reliable facts.
Corroborated	Data should be backed up by evidence.

10.5 Study Record Retention

The principal investigator is required to maintain adequate records of the disposition of the product, including dates, quantity and use by subjects, as well as written records of the disposition of the product when the study ends.

The principal investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational product or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

Study documentation includes all CRFs, data correction forms or queries, source documents, sponsor-investigator correspondence, monitoring logs/letters, and regulatory documents (e.g., protocol and amendments, IRB correspondence and approval, signed patient consent forms).

Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study.

In accordance with FDA regulations, the investigator shall retain records for a period of two years following the date a marketing application is approved for the product for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified.

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APPENDIX 1. *FITBIT PRODUCT INFORMATION*

Informational Video

https://youtu.be/eNbozxFz3oA?list=PL_xLGCqFuhiERByEP1f6YWCAtYiaTBLY8

Sync Information

Fitbit Help > How do Fitbit devices sync their data?

How do Fitbit devices sync their data?

This article explains how to save the data your device collects in your Fitbit account.

SKIP TO:

- What is syncing?
- When does my tracker or watch sync?
- How do I manually sync my tracker or watch?
- When does my scale sync?
- Where can I see when my device last synced?
- Why can't I sync my device?
- Will syncing work with my phone, tablet, or computer?
- How often should I sync my tracker or watch?
- Can I sync my tracker or watch with more than one device?
- Can I sync more than one Fitbit device to the same account?

Sleep Information

How do I track my sleep with my Fitbit device?

Fitbit helps you better understand your sleep patterns and quality with different sleep tools.

Skip to:

- What do the different sleep states mean in the Fitbit app?
- How do I see my sleep data in the Fitbit app?
- How is my time asleep calculated in the Fitbit app?
- How does my Fitbit device automatically detect sleep?
- How do I change my sleep goal in the Fitbit app?
- How do I manage sleep insights in the Fitbit app?
- How do I set a sleep schedule in the Fitbit app?
- How do I set a bedtime reminder in the Fitbit app?
- Can my Fitbit device log a nap?
- How do I edit my sleep history in the Fitbit app?
- What is the difference between the normal and sensitive sleep setting in the Fitbit app?

CYSTIC FIBROSIS FOUNDATION

CFF FINAL SCIENTIFIC REPORT
FACE PAGE

Type of Award:	**CFF Award #:** FRANCO19KO	
Principal Investigator (PI):	Rose A. Franco, MD	
Institution:	The Medical College of Wisconsin, Inc	
Project Title:	STeP IT UP CF: Stiulating improved Health and wellbeing in Cystic Fibrosis	
PI's Contact Information:	**Mailing Address:** Department of Medicine The Medical College of Wisconsin 9200 West Wisconsin Avenue Milwaukee, WI 53226	**Department:** Medicine **Email:** rfranco@mcw.edu **Telephone:** 414-955-7040

PRINCIPAL INVESTIGATOR AND INSTITUTIONAL ASSURANCES

Invention Disclosures/Patents?	x **No,NA** ☐ **Yes, all relevant invention disclosure and/or patent information is included in this final report.**

Assurance Statement: We, the undersigned, certify that the statements herein are true and complete to the best of our knowledge and accept the regulations, policies, and objectives of the Cystic Fibrosis Foundation concerning this type of project.

(CFF accepts digital signatures that are verifiable. Please note: Principal Investigator & Authorized Institutional Official's Signatures are required)

_____

Principal Investigator's Signature / Date

_____

Mentor's Signature (if applicable) / Date

Mentor's Name: _____

_____

Authorized Institutional Official's (AIO) Signature / Date

AIO's Name: _____

Title: _____

Email & Telephone: _____