C3 Translational Core

CJ Nemastil, BA, BS
August 7, 2019

Nationwide Children's
When your child needs a hospital, everything matters.℠

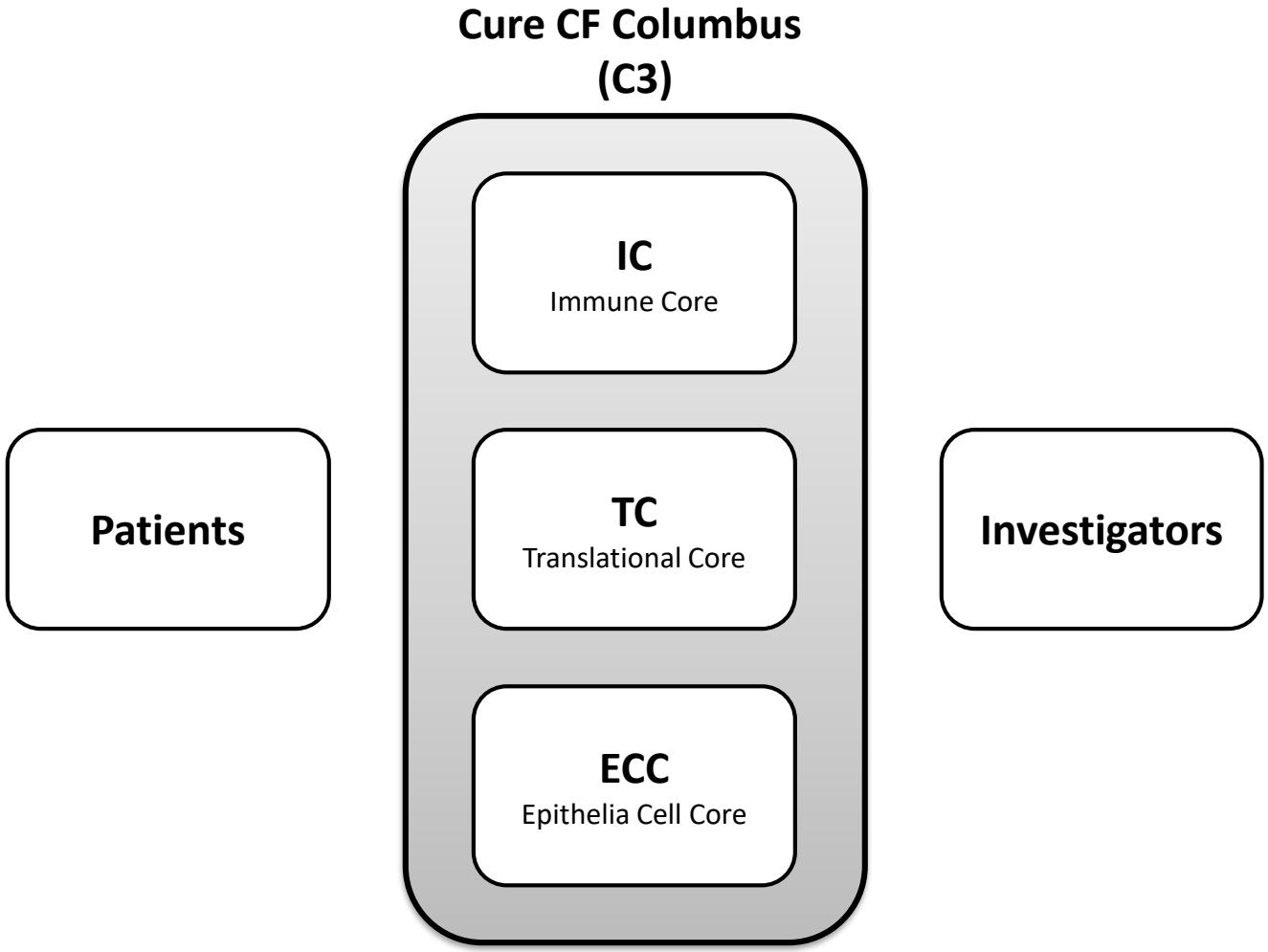
C3 Cure Cystic Fibrosis Columbus

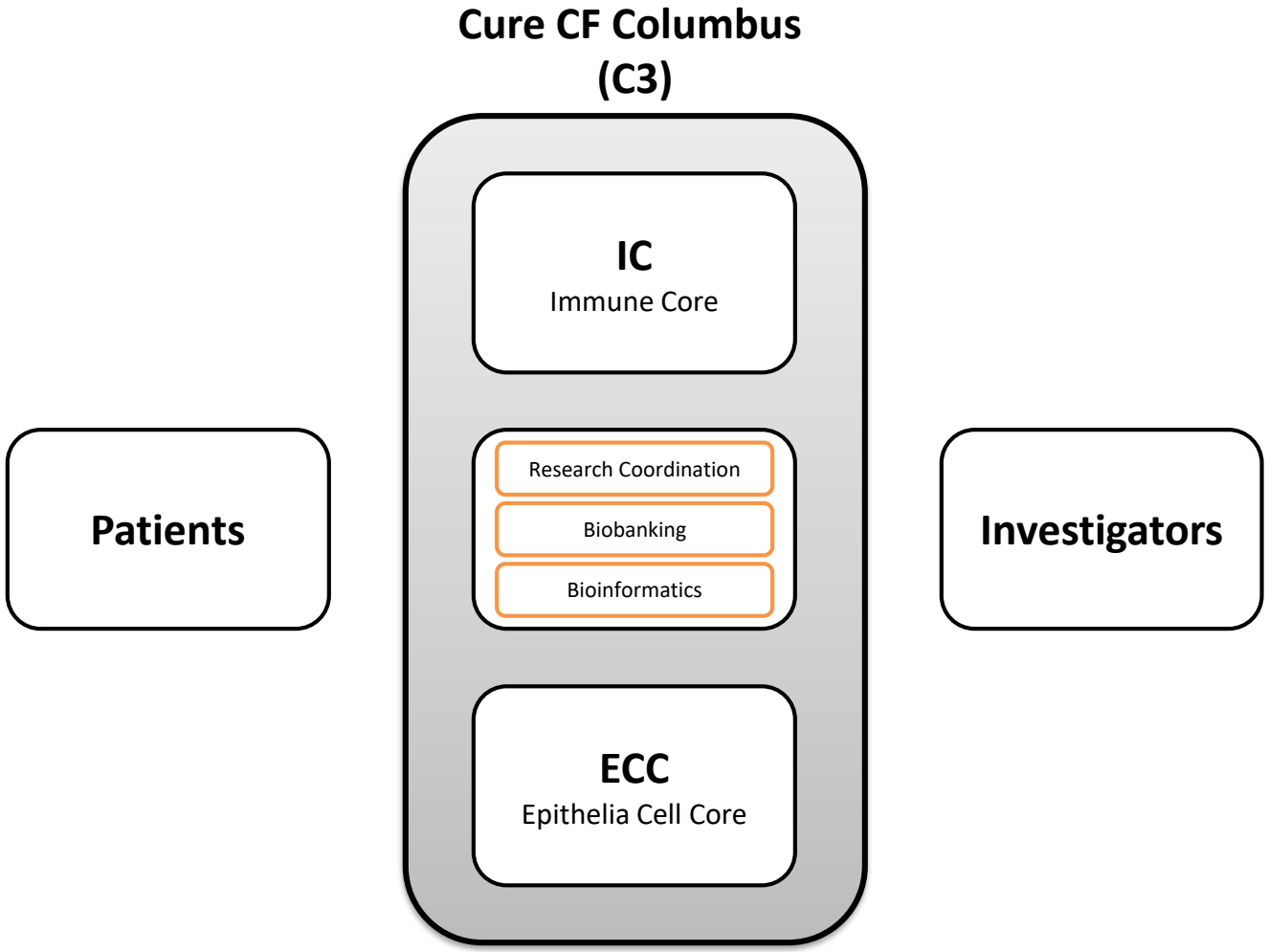
The Ohio State University

Patients

Cure CF Columbus (C3)

Investigators


Cure CF Columbus
(C3)
IC
Immune Core
TC
Translational Core
ECC
Epithelia Cell Core
Patients
Investigators


Cure CF Columbus
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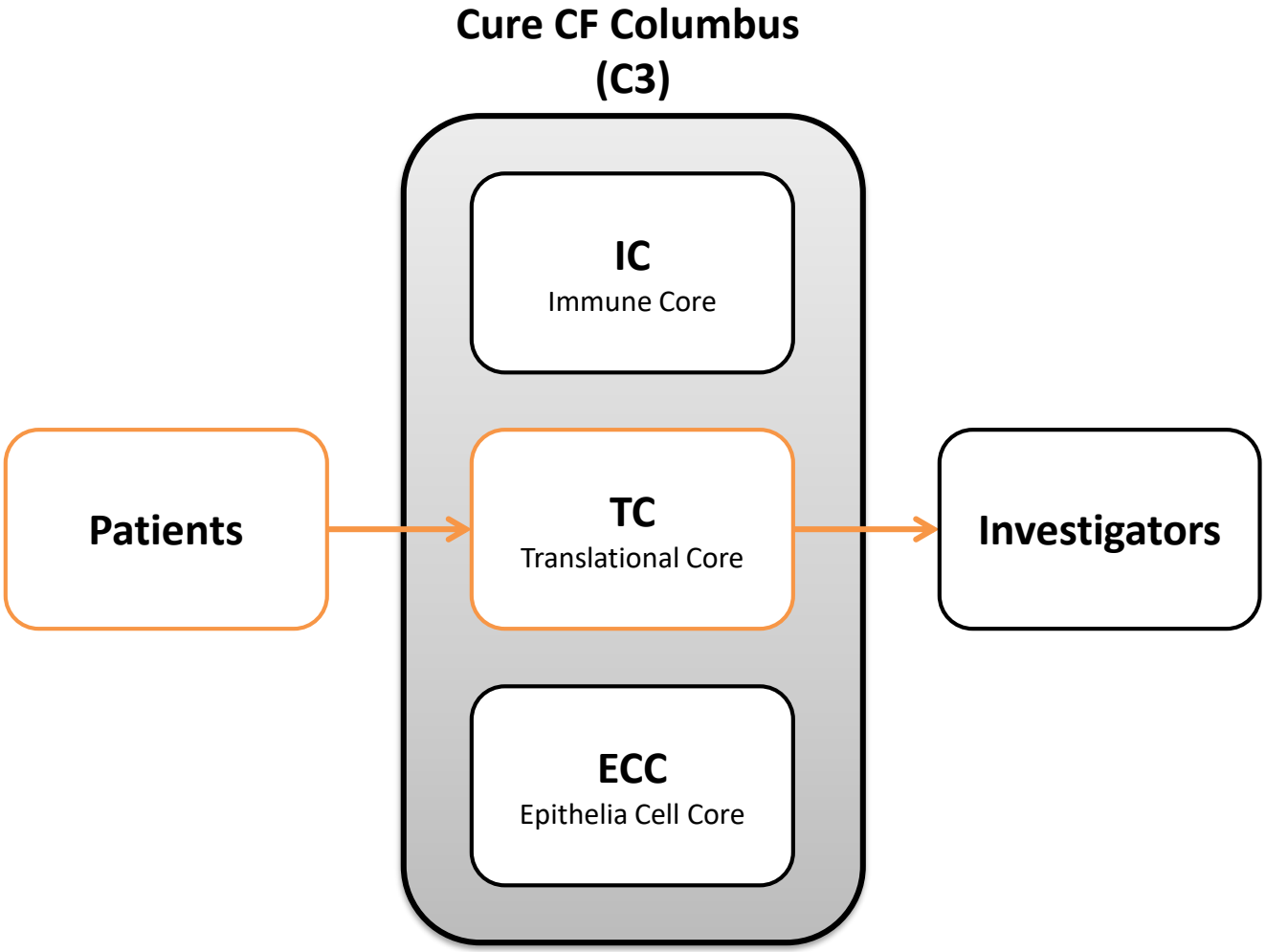
Research Coordination
Biobanking
Bioinformatics
ECC
Epithelia Cell Core
Patients
Investigators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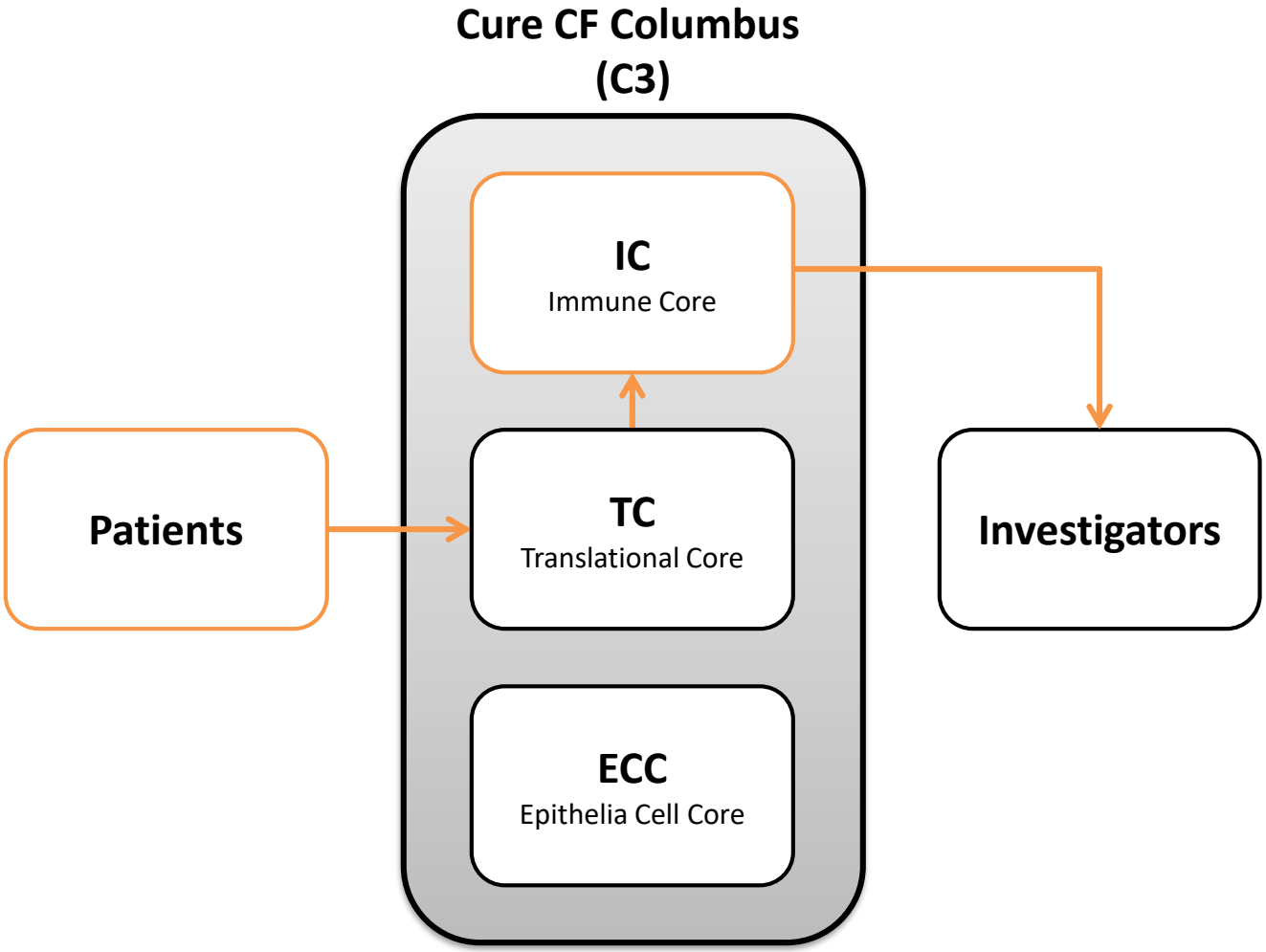
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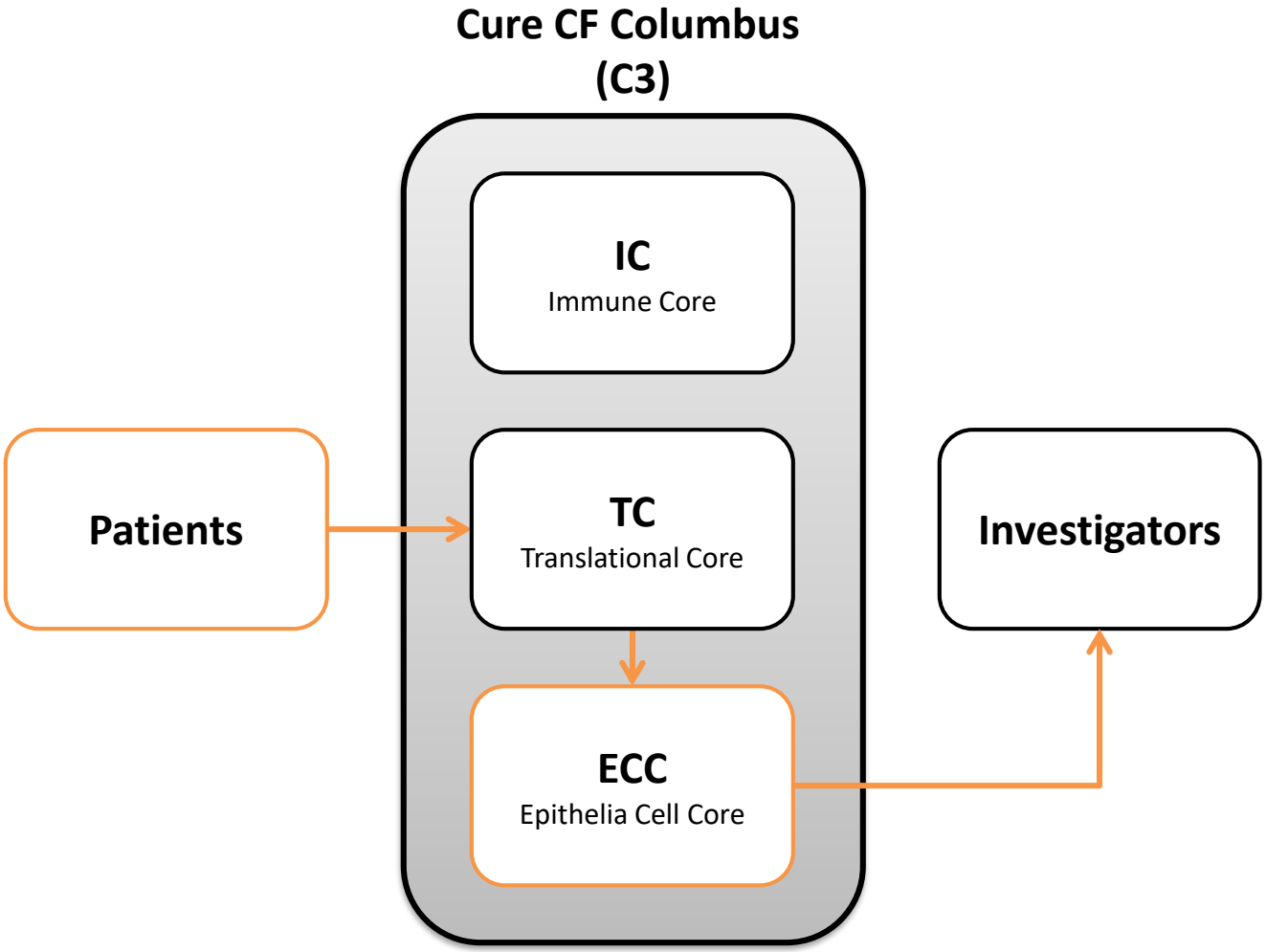
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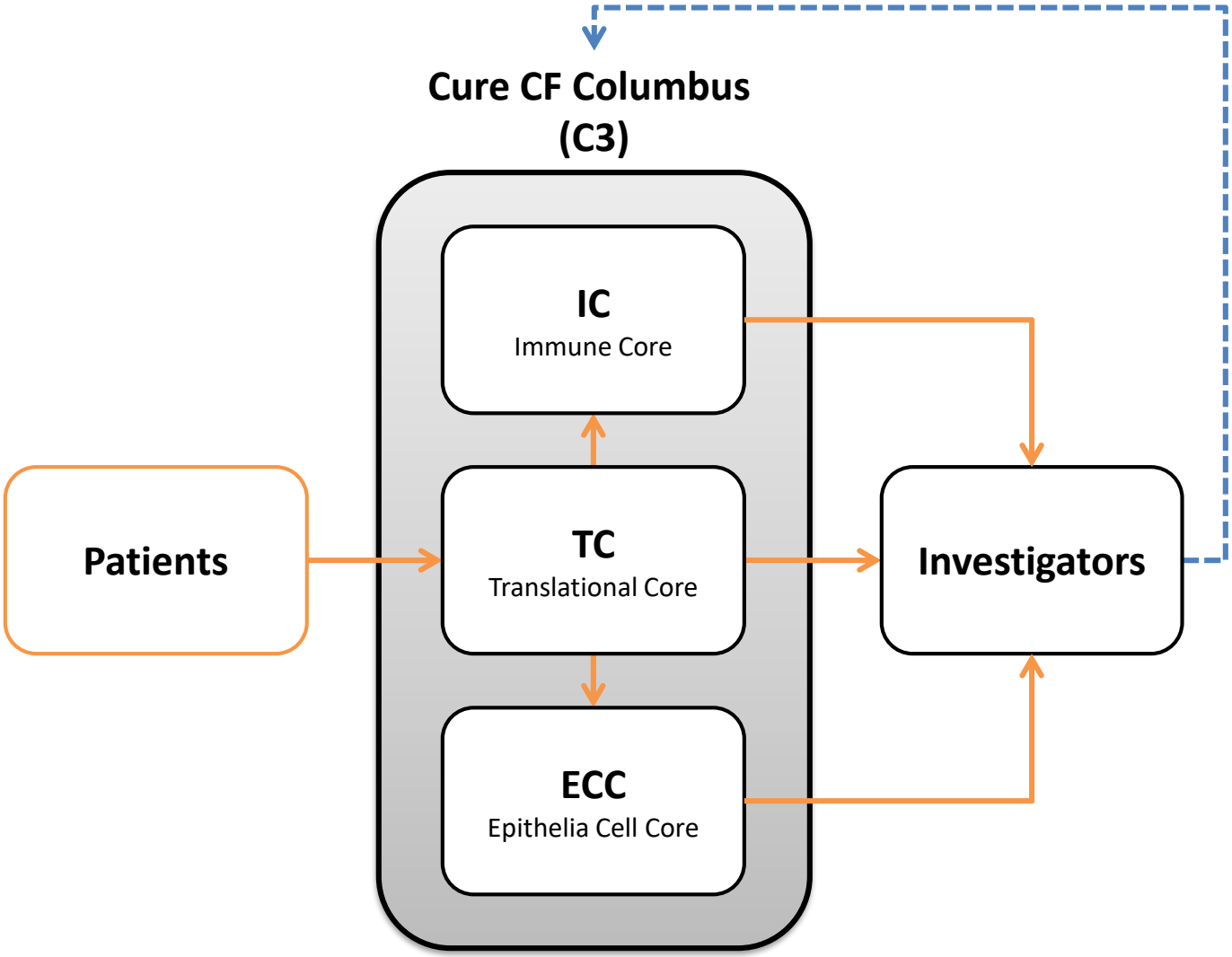
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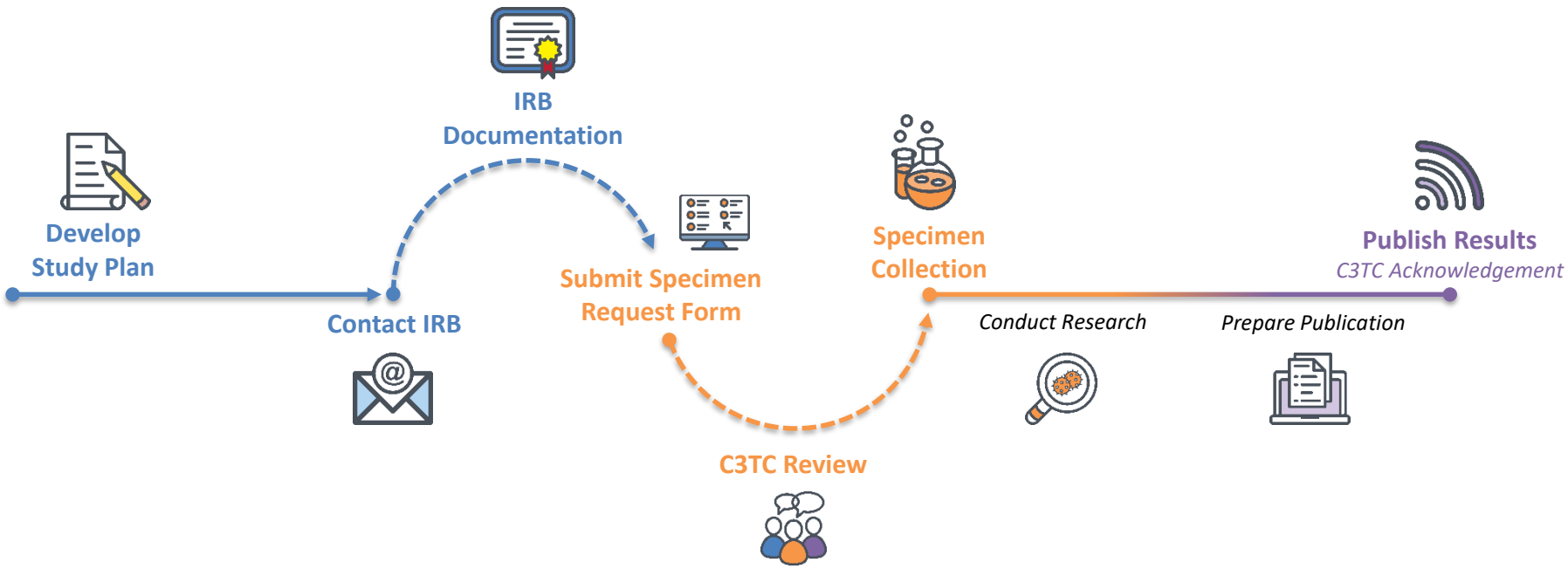
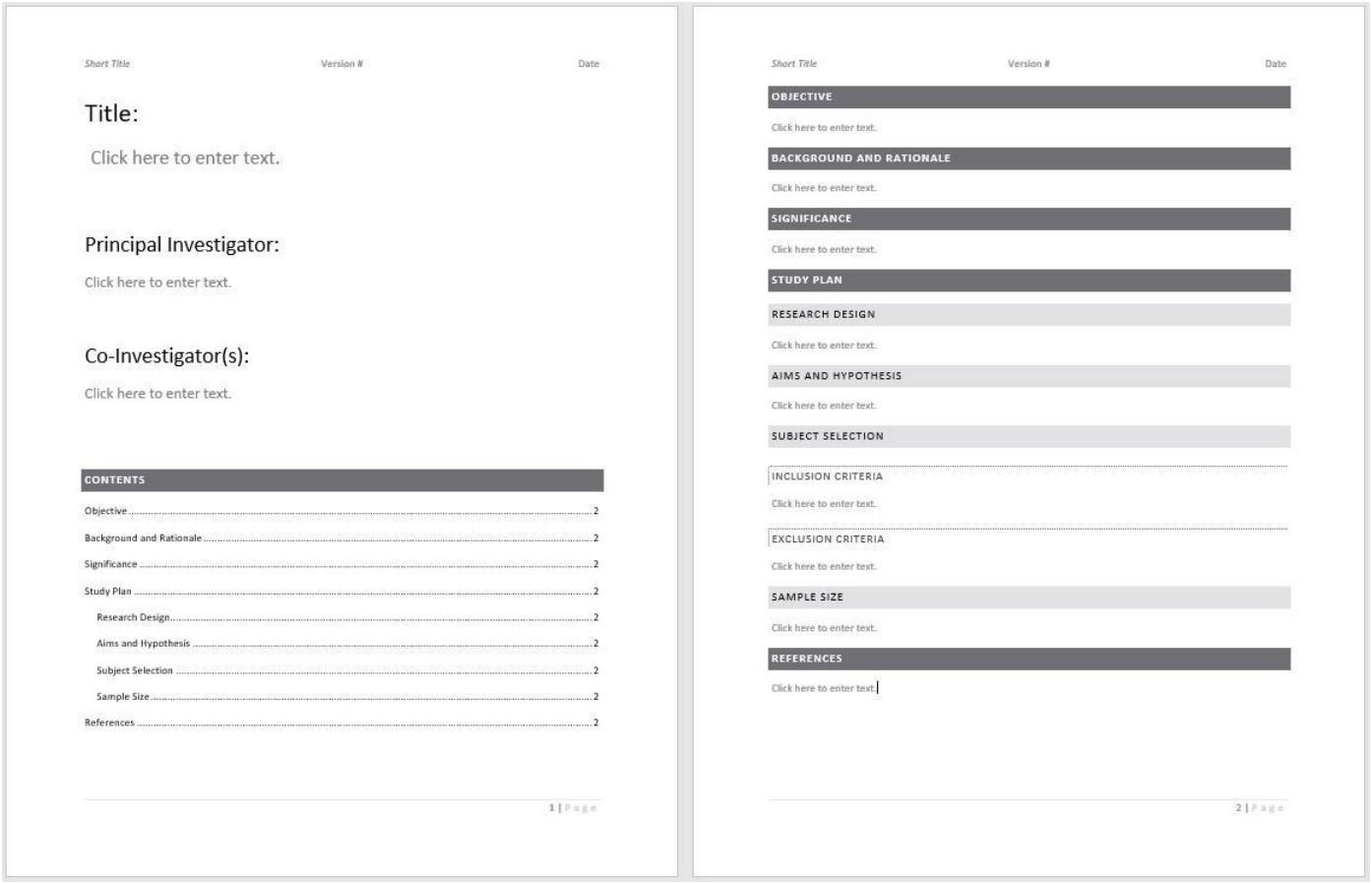
Specimen Requests



Develop Study Plan



Short Title Version # Date

Title:

Click here to enter text.

Principal Investigator:

Click here to enter text.

Co-Investigator(s):

Click here to enter text.

CONTENTS

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Short Title Version # Date

OBJECTIVE

Click here to enter text.

BACKGROUND AND RATIONALE

Click here to enter text.

SIGNIFICANCE

Click here to enter text.

STUDY PLAN

RESEARCH DESIGN

Click here to enter text.

AIMS AND HYPOTHESIS

Click here to enter text.

SUBJECT SELECTION

INCLUSION CRITERIA

Click here to enter text.

EXCLUSION CRITERIA

Click here to enter text.

SAMPLE SIZE

Click here to enter text.

REFERENCES

Click here to enter text.

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IRB

Email to your institutional IRB

- Seeking a determination of exempt status
- Receiving de-identified specimens and/or data from C3Biobank (NCH IRB16-00730)
- Attach a copy of your Study Plan

Study deemed exempt

- Email response from IRB serves as IRB Documentation

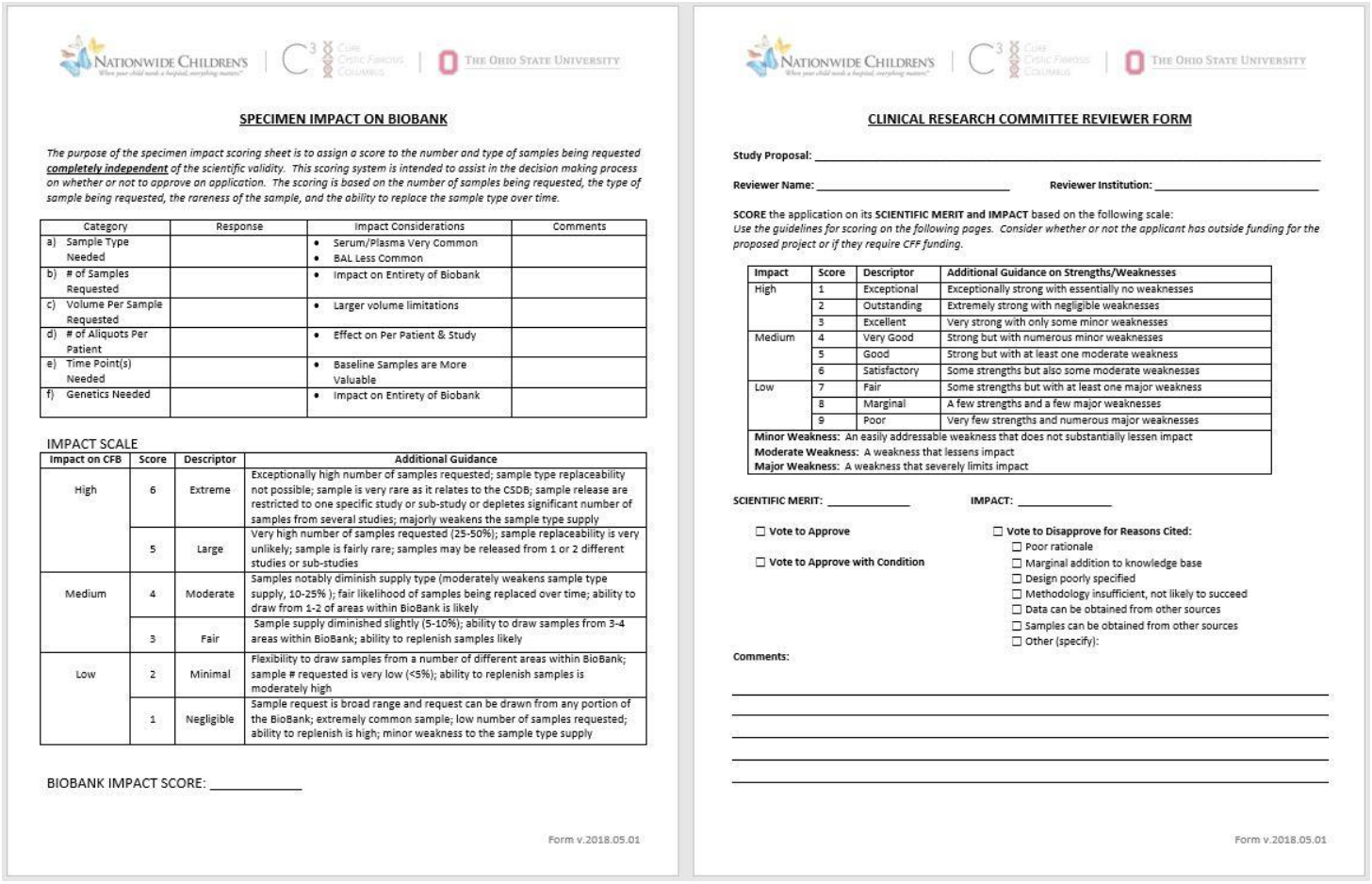
Submit Specimen Request Form

Links on www.CureCFColumbus.org

- Top of Core Services webpage
- Top of Translational Core webpage
- Bottom of Immune Core webpage

CURE CF COLUMBUS

C3TC Specimen Request Review Board



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SPECIMEN IMPACT ON BIOBANK

*The purpose of the specimen impact scoring sheet is to assign a score to the number and type of samples being requested **completely independent** of the scientific validity. This scoring system is intended to assist in the decision making process on whether or not to approve an application. The scoring is based on the number of samples being requested, the type of sample being requested, the rareness of the sample, and the ability to replace the sample type over time.*

Category	Response	Impact Considerations	Comments
a) Sample Type Needed		• Serum/Plasma Very Common • BAL Less Common	
b) # of Samples Requested		• Impact on Entirety of Biobank	
c) Volume Per Sample Requested		• Larger volume limitations	
d) # of Aliquots Per Patient		• Effect on Per Patient & Study	
e) Time Point(s) Needed		• Baseline Samples are More Valuable	
f) Genetics Needed		• Impact on Entirety of Biobank	

IMPACT SCALE

Impact on CFB	Score	Descriptor	Additional Guidance
High	6	Extreme	Exceptionally high number of samples requested; sample type replaceability not possible; sample is very rare as it relates to the CSDB; sample release are restricted to one specific study or sub-study or depletes significant number of samples from several studies; majorly weakens the sample type supply
	5	Large	Very high number of samples requested (25-50%); sample replaceability is very unlikely; sample is fairly rare; samples may be released from 1 or 2 different studies or sub-studies
Medium	4	Moderate	Samples notably diminish supply type (moderately weakens sample type supply, 10-25%); fair likelihood of samples being replaced over time; ability to draw from 1-2 of areas within BioBank is likely
	3	Fair	Sample supply diminished slightly (5-10%); ability to draw samples from 3-4 areas within BioBank; ability to replenish samples likely
Low	2	Minimal	Flexibility to draw samples from a number of different areas within BioBank; sample # requested is very low (<5%); ability to replenish samples is moderately high
	1	Negligible	Sample request is broad range and request can be drawn from any portion of the BioBank; extremely common sample; low number of samples requested; ability to replenish is high; minor weakness to the sample type supply

BIOBANK IMPACT SCORE: _____

Form v.2018.05.01

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CLINICAL RESEARCH COMMITTEE REVIEWER FORM

Study Proposal: _____

Reviewer Name: _____ **Reviewer Institution:** _____

SCORE the application on its **SCIENTIFIC MERIT and IMPACT** based on the following scale:
Use the guidelines for scoring on the following pages. Consider whether or not the applicant has outside funding for the proposed project or if they require CFF funding.

Impact	Score	Descriptor	Additional Guidance on Strengths/Weaknesses
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Medium	4	Very Good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but with at least one major weakness
	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths and numerous major weaknesses

Minor Weakness: An easily addressable weakness that does not substantially lessen impact
Moderate Weakness: A weakness that lessens impact
Major Weakness: A weakness that severely limits impact

SCIENTIFIC MERIT: _____ **IMPACT:** _____

☐ **Vote to Approve**

☐ **Vote to Approve with Condition**

☐ **Vote to Disapprove for Reasons Cited:**
- ☐ Poor rationale
- ☐ Marginal addition to knowledge base
- ☐ Design poorly specified
- ☐ Methodology insufficient, not likely to succeed
- ☐ Data can be obtained from other sources
- ☐ Samples can be obtained from other sources
- ☐ Other (specify):

Comments:

_____
_____
_____
_____
_____

Form v.2018.05.01

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Specimen Collection

PatientUSI	Barcode	Timepoint	SpecimenType	TubeType	Units	Protocols
AAAAAA	0ABC01	TraC-002	Blood Fresh	EDTA	10 mL	CF Bank
AAAAAA	0ABC02	TraC-002	Blood Fresh	EDTA	10 mL	CF Bank
AAAAAA	0ABC03	TraC-002	Blood Fresh	EDTA	5 mL	CF Bank
AAAAAA	0ABC04	TraC-002	Blood Fresh	Tempus	1 mL	CF Bank

Total Number of Specimens	4

Shipping Contact	Billing Information	Tracking Number
Researcher's Name		N/A
Researcher's Institution		Courier Service
Address 1		In House
Address 2		Fedex Account#
Address 3		
Phone Number		P.O. Number
Email Address		

Data Reports

Demographics										
Request ID	**USI**	**Barcode**	**Specimen Type**	**Units**	**GENDER**	**AGE**	**GENE 1**	**GENE 2**	**Race**	**Insurance Type**
TraC-002	AAAAAA	0ABC01	Blood Fresh	10 mL	Female	24	F508del	F508del	Caucasian	CareSource
TraC-002	AAAAAA	0ABC02	Blood Fresh	10 mL	Female	24	F508del	F508del	Caucasian	CareSource
TraC-002	AAAAAA	0ABC03	Blood Fresh	5 mL	Female	24	F508del	F508del	Caucasian	CareSource
TraC-002	AAAAAA	0ABC04	Blood Fresh	1 mL	Female	24	F508del	F508del	Caucasian	CareSource

Age

Patient age in years at time of specimen collection.

Gene 1 & 2

Patient's CFTR gene mutations (N/A for control patients).

Data Reports

Flowsheet					
USI	**Measure**	**Most Recent**	**Value Day of Collection**	**Min**	**Max**
AAAAAA	%FEV1	56	Yes	50	69
AAAAAA	BMI	21.69	No	20	23.1

Most Recent
Most recent value reported up to, and including, the date of collection.

Value Day of Collection

Yes Most recent value is from the same day as collection.

No Most recent value is from a date prior to the collection date.

Min
Lowest value reported within one year of the collection date.

Max
Highest value reported within one year of the collection date.

CFTR Modulator Use		
USI	**Type**	**Last Use**
AAAAAA	lumacaftor/ivacaftor	> 1 year

Last Use
Period of time patient has been off CFTR modulator if taken previously.

Current
< 1 month
> 1 month
> 6 months
> 1 year
> 2 years
No Record

Data Reports

Organisms										
USI	**Organism**	**Present Day of Collection**	**Amikacin**	**Aztreonam**	**Cefepime**	**Ceftazidime**	**Ciprofloxacin**	**Gentamicin**	**Meropenem**	**Tobramycin**
AAAAAA	PSEUDOMONAS AERUGINOSA	Yes	R	R	R	R	R	R	R	S

USI	**Organism**	**Present Day of Collection**	**Clindamycin**	**Doxycycline**	**Erythromycin**	**Gentamicin**	**Linezolid**	**Nafcillin**	**Trimethoprim/ sulfamethoxazole**	**Vancomycin**
AAAAAA	STAPHYLOCOCCUS AUREUS	Yes	R	S	R	S	S	S	S	S

Organism

Lists organisms that have be cultured within one year of the collection date.

Present Day of Collection

Yes	Culture labs were performed on the same day as specimen collection AND the organism was cultured.
No	Culture labs were performed on the same day as specimen collection AND the organism was NOT cultured.
Unk	Culture labs were NOT performed on the same day as specimen collection.

Key

S	Susceptible
I	Intermediate
R	Resistant

Publish Results

C3TC Acknowledgement:

The members of Cure CF Columbus Translational Core (C3TC) include: Dr. Karen McCoy, CJ Nemastil, Terri Johnson, Melinda Smith, Laura Raterman, Patti Olson, and April Hunt. C3TC is supported by the Division of Pediatric Pulmonary Medicine, the Biopathology Center Core, and the Data Collaboration Team at Nationwide Children's Hospital. Grant support provided by The Ohio State University Center for Clinical and Translational Science (National Center for Advancing Translational Sciences, Grant UL1TR002733) and by the Cystic Fibrosis Foundation (Research Development Program, Grant MCCOY19RO).

Step 1

Develop Study Plan

Write a ***Study Plan***, which includes a full description of the proposed research study.

Resource: Study Plan Template (see Resources)

Step 2

Contact IRB

Send an email to your institutional IRB. State that you are seeking a determination of exempt status for your study. Make sure to include a copy of your ***Study Plan***.

IRB Website: Nationwide Children's Hospital
The Ohio State University

IRB Documentation

Research may begin once you receive an email from the IRB stating your research is exempt.

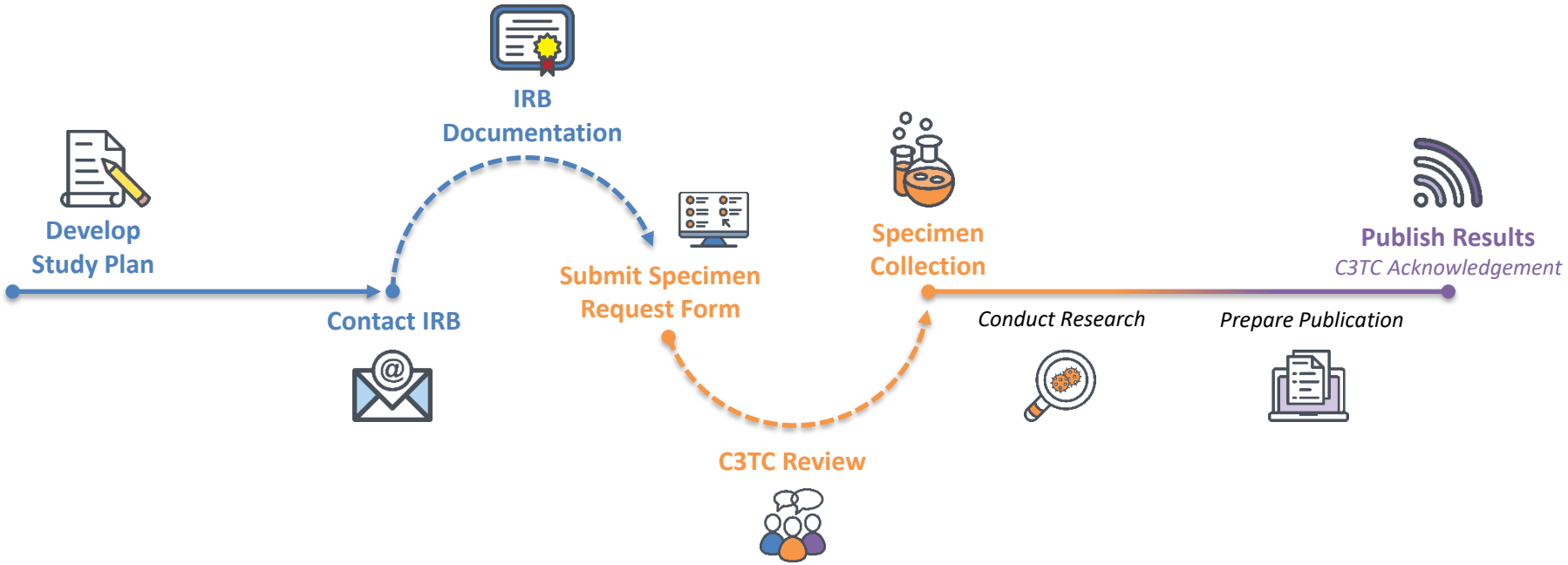
This email serves as ***IRB Documentation***.

Step 3

Submit Specimen Request Form

Complete the online form to initiate the specimen request process. The ***Study Plan*** **MUST** be included with your submission. Request can be submitted without ***IRB Documentation***, but **WILL NOT** be approved until documentation is provided.

Resource: C3TC Specimen Request Form



C3TC Review

Approval will be granted based on ***feasibility*** (type, timeframe, and number of specimens required) and overall ***scientific merit*** as determined by the C3TC Specimen Request Review Board (SRRB).

Resource: Impact on C3Biobank
Scientific Merit & Impact
(see Resources)

Specimen Collection

Once approved by the SRRB, the C3TC works with the primary contact, as noted on the ***Specimen Request Form***, to arrange collection and/or delivery of specimens and data.

Publish Results

Publications resulting from studies supported by the C3TC should include the following acknowledgement:

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Tentative Cost

If you have questions about pricing, please contact:

CJ Nemastil

CJ.Nemastil@nationwidechildrens.org

(614)722-2115

Funding Opportunities:

CCTS Core Services Voucher Support

C3 Website

CURE CF COLUMBUS

Questions?


NATIONWIDE CHILDREN'S
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C3
CURE
CYSTIC FIBROSIS
COLUMBUS


THE OHIO STATE UNIVERSITY

Cure CF Columbus (C3)

Is Now C3RDP

Karen S .McCoy, MD
August 7, 2019

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Updates Planned

Status of C3RDP

Translational Core (C3TC)

Highlights of Clinical Research

Questions and Answers

It's Been a Big Year

- We have been designated as an RDP
- We received $500,000 per year for four years
- All cores and both pilots were funded

  Epithelial **C**ell **C**ore

  Immune **C**ell **C**ore

  C3 **T**ranslational **C**ore
- There are also other funding opportunities exclusively available to RDP sites

Pulmonary Research Core (PRC) Reorganization

Linda Humston, Associate Director

- April Hunt, Regulatory Coordinator
- Beth Skaggs, Regulatory Coordinator
- CJ Nemastil, Data Analyst/Honest Broker
- 2 Non-clinical RC

- Terri Johnson, RN, Research Coordinator
- Laura Raterman, RN, Research Coordinator
- Patti Olson, RN, Research Coordinator
- Melinda Smith, RN, Research Coordinator

- Monitor Grant Financials
- All regulatory work
- Track patient activity: clinic, procedures, inpatient, transplant, consent status
- Access sample/transit process

Background on Sample Handling

All specimens collected by/for C3RDP investigators must be checked into C3TC

Enduring IRB for collections target all CF patients and suitable controls

Data Use Agreement/Material Transfer Agreement ➡ are covered ONLY by C3TC

Process

C3TC Specimens acquire a unique specimen identifier (de-identifies the actual specimen, but we maintain the secure ability to retrieve)

Investigators in C3 can get specimens if they do not want clinical data requiring only the C3TC IRB/consent, but should email your IRB and verify

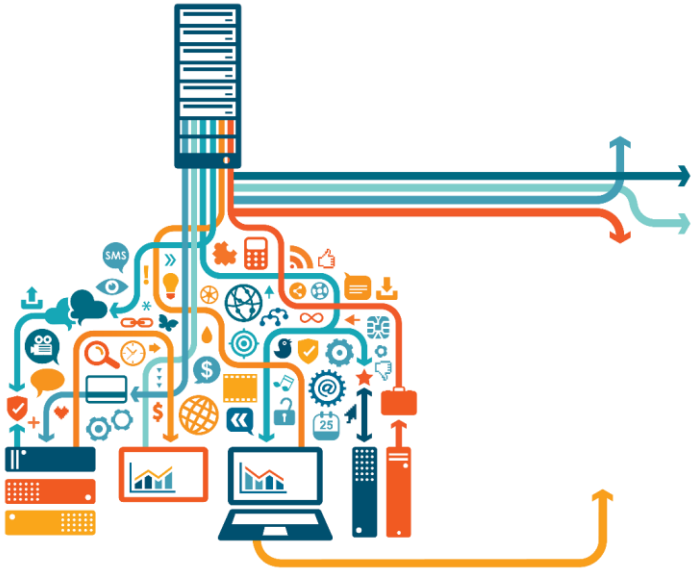
After de-identification, we can still anonymously pull back the information related to the specimen's patient characteristics through our honest broker

Investigators in C3 can get these characteristics with an IRB waiver letter (exception of lung transplantation)

Plans Going Forward

Next stage of this operation is creation of an automated data pull capability from EPIC (EMR)

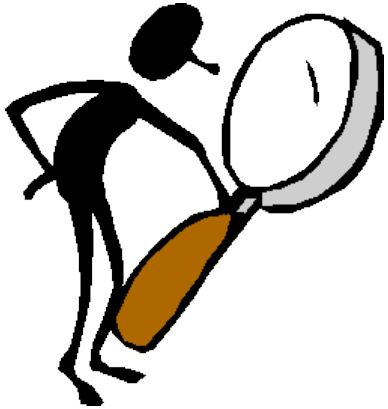
This will allow individual investigators to retrieve de-identified clinical characteristics to go with their specimen through the honest broker



And It Has Been a Big Year in Clinical Research!

Triple Combination

Highlights of Clinical Research



Triple combination therapy in F508del homozygotes

(VX445/TEZ/IVA)

(Elexacaftor/Tezacaftor/Ivacaftor)

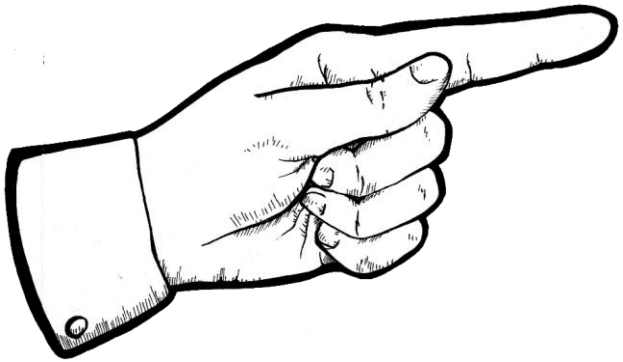
Has been submitted to FDA for use in CF F508del homozygotes or heterozygotes with the other gene a minimal function type

Press Release

- Comparison of 445/TEZ/IVA to Placebo/TEZ/IVA
- Each group got a 4 week run in of Symdeko (TEZ/IVA)

Then randomized to receive a 4 week trial
445/TEZ/IVA vs Placebo/TEZ/IVA

Primary End Point



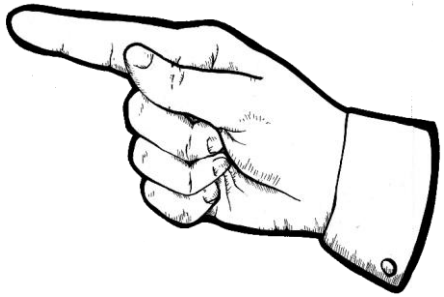
Absolute change pp FEV1, percent predicted lung function

445/TEZ/IVA (55 subjects) vs Placebo/TEZ/IVA (52 subjects)

Net increase of **10% (14 for total period from start of run in**) relative to placebo/TEZ/IVA no change, p<0.0001

Secondary End Points

Absolute change mmol/L
Sweat Chloride
445/TEZ/IVA **45.1 p<0.0001**
Placebo/TEZ/IVA no change



All SwCl values below diagnostic threshold for CF

Change in CFQ6R-RD validated quality of life score with minimal clinically important difference (MCID) + 4 points

445/TEZ/IVA **+17.4 points p<0.0001**
Placebo/TEZ/IVA No change

Additional Important Changes

Nutritional End Points:

445/TEZ/IVA- both BMI and Body Weight improved, while no change in Placebo/TEZ/IVA group (in just 4 weeks)

No significant safety findings

No discontinuations were necessary for adverse events

Implications of this drug for C3RDP

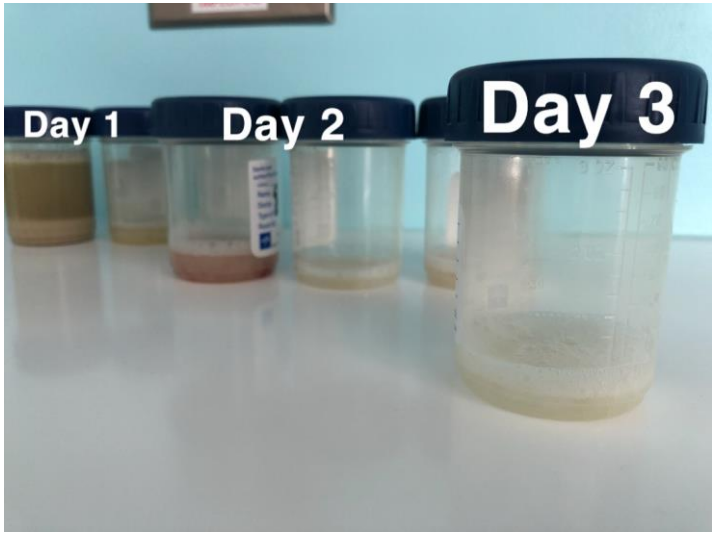
- Huge it is able to change respiratory health, sweat chloride, and quality of life in hours to days
- Timing: The FDA clock is ticking, we need to be ready now
- Focus on pre-post changes relevant to cellular function, etc
- Focus on analysis related to immune dysfunction and infection

The population:

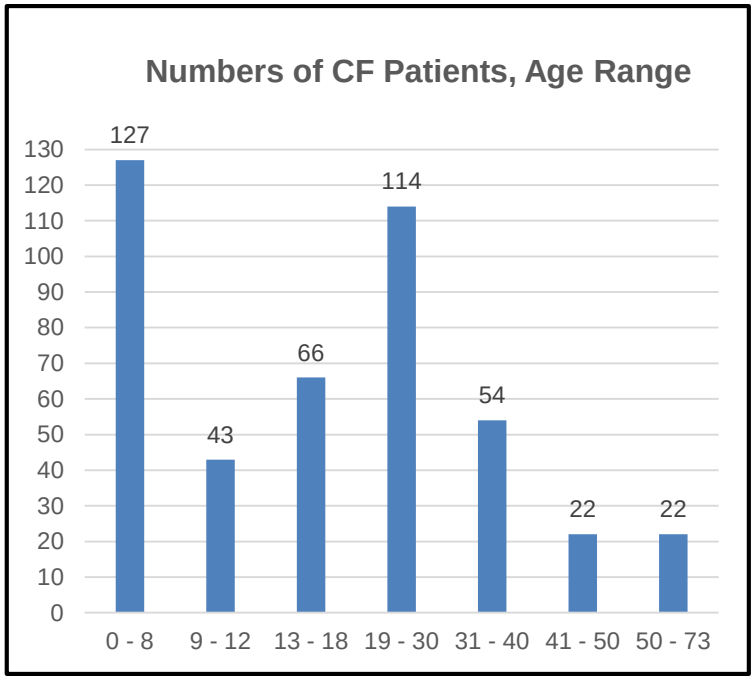
< 12 years are just beginning study

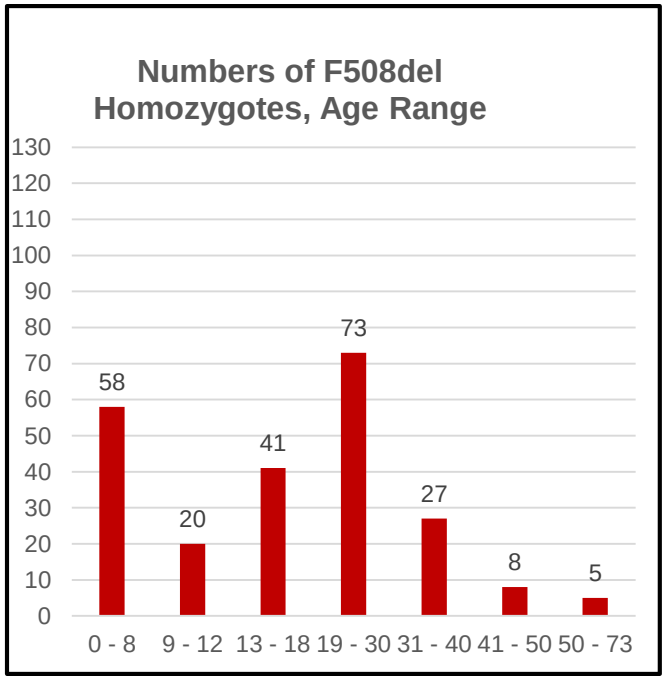
< 6 years not studying yet

< 2 years not studying yet



CF Population by Age Group and Characteristics





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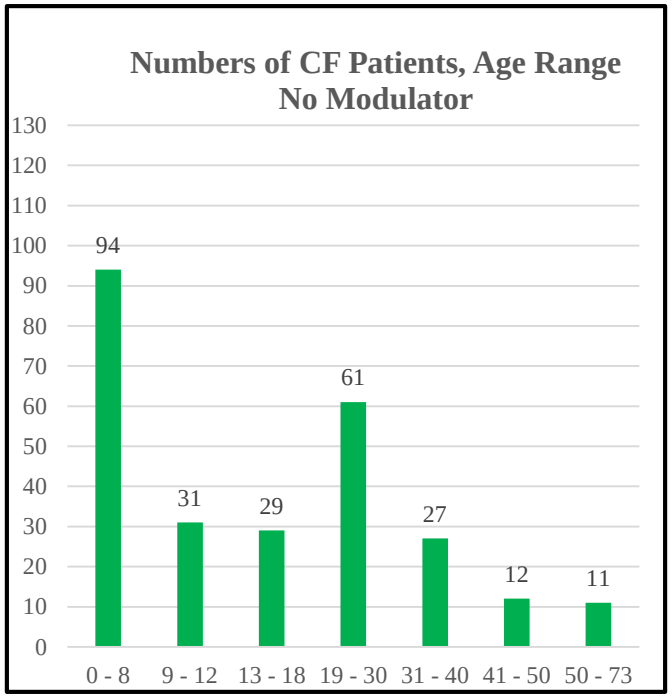
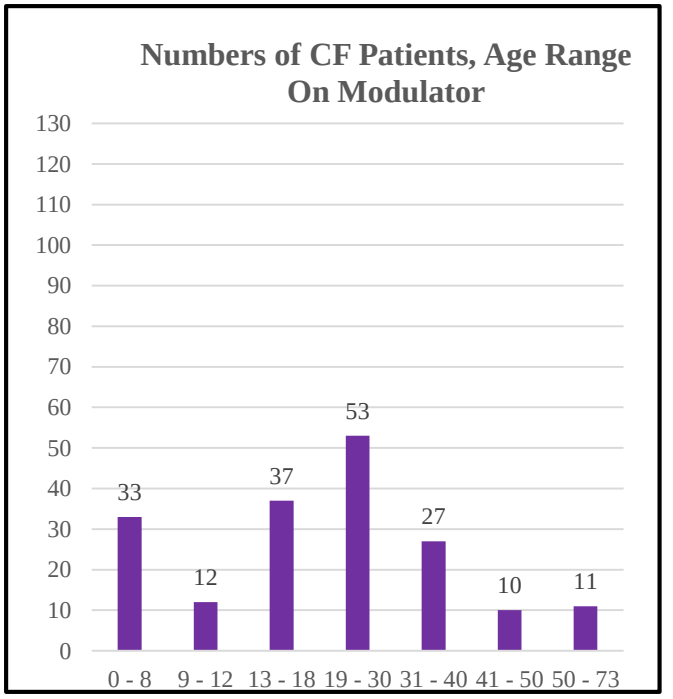
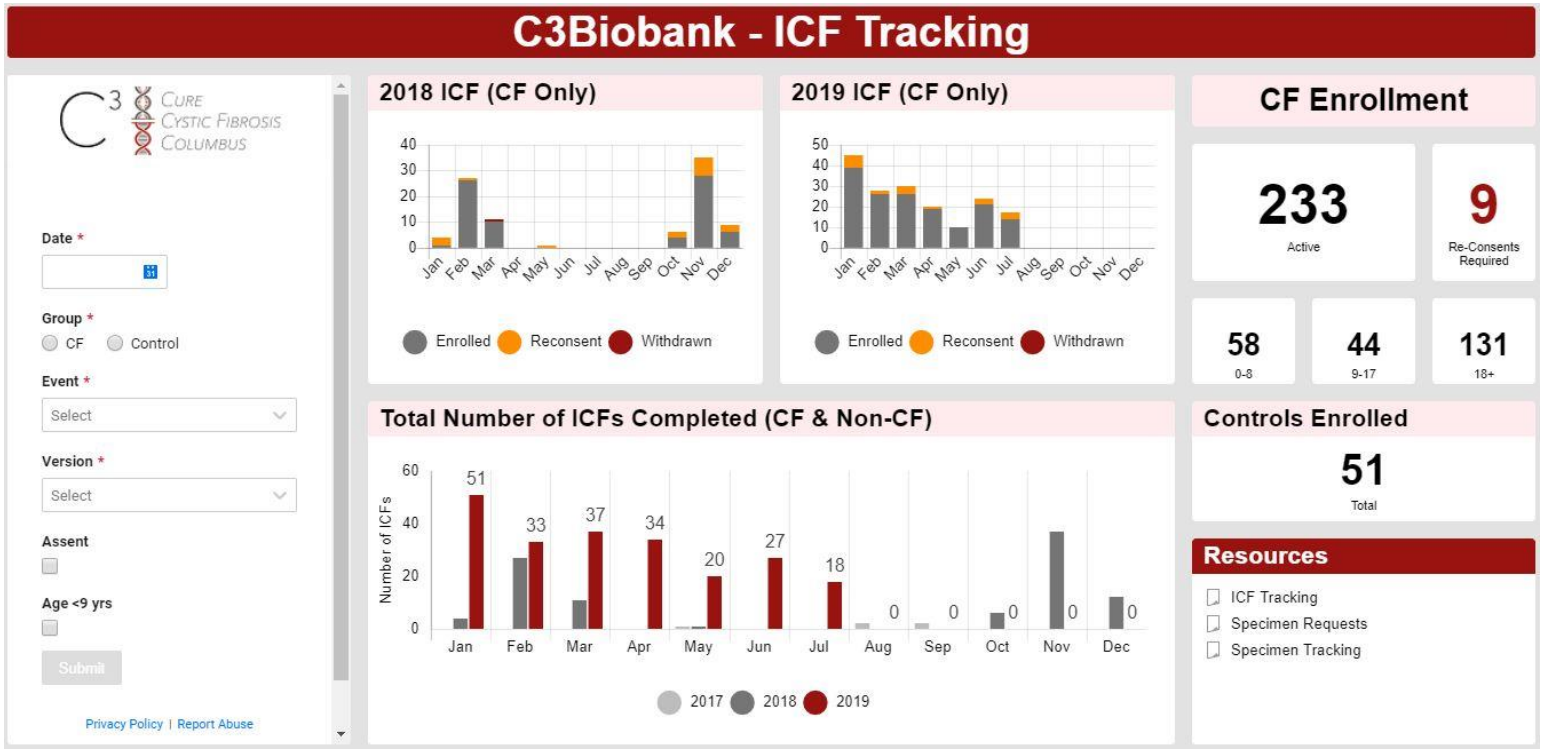




ICF Tracking



Questions?