Pediatric Influence of Cooling duration on Efficacy in Cardiac Arrest Patients

Investigator Meeting
Friday, May 6

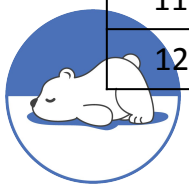
P-ICECAP

NIH SIREN
Emergency
Trials
Network

Good Morning!

Agenda

Time	Topic	Speaker
7:15 AM	**Breakfast**	
7:45 AM	Milestones & Finance	Valerie Stevenson, BAS, RRT, CCRP
7:55 AM	Regulatory Readiness	Carol Van Huysen
8:25 AM	Ancillary Study Ideas	Dr. Alexis Topjian, MD
9:10 AM	Publications	Dr. Frank Moler, MD
9:30 AM	SIREN Website orientation	Courtney Miller, LMSW & Carol Van Huysen
9:45 AM	Break - Hotel Checkout	
10:00 AM	Protocol and Standardization Game - Kahoot!	Dr. William Meurer, MD, & Moni Weber, RN, BSN, CCRP
11:00 AM	**Open Forum Q and A**	Dr. Frank Moler, MD, Dr. Alexis Topjian, MD, & Dr. William Meurer, MD
12:00 PM	Adjourn Day 3	



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Milestones & Finance

Valerie Stevenson

Start-up Payment

- A one-time payment of **$5000 (inclusive of F&A costs)** will be paid to up to forty (40) P-ICECAP sites upon the completion of all required trainings, regulatory documents submission, institutionally required approvals, signed and executed contracts and are *released to enroll* subjects by the Clinical Coordinating Center.

- Start-up funds are *reduced by $1,000* per calendar month if all start-up requirements are completed after the posted deadline. Sites not included in the original proposal may not be eligible for this start-up payment.

Per-subject Payments

Milestone	I	II	III	IV	V	V a	V b
	Screening stipend	Enrolled, died during hospitalization OR alive at discharge stipend	3 Month (VABS III) stipend	12 month (VABS III) stipend	12 Month Neurological Appointment scheduled and successfully completed stipend	12 Month Neurological exam by Neurologist stipend	12 Month Family expenses for travel to neurological exam
PAYMENT AMOUNT	**$100**	**$7,000**	**$1,000**	**$2,000**	**$500**	**$500**	**$150**

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Per-subject Payments

- Sites that are open to enroll will be eligible for subject payment of **$7,000 (inclusive of F&A costs)** after an eligible subject is enrolled and randomized and all study CRFs required from baseline through hospital discharge are **submitted and free of queries**. This includes subjects that died prior to discharge.

- Sites will be eligible for a second subject payment for the 3 Month (VABS III) visit of **$1,000 (inclusive of F&A costs)** when the visit is successfully completed and all required study CRFs **are submitted and free of queries**.

- Sites will be eligible for a third and final subject payment of a maximum of **$3,150 (inclusive of F&A costs)** when the visit is successfully completed and all required study CRFs **are submitted and free of queries**.
  - Included in the maximum payment is $2,000 for completion of the 12 month (VABS III), $500 for scheduling and completing the Neurological exam, $500 payment once the neurology exam is completed and $150 for subject reimbursement for travel expenses

Per-subject Payments

- Sites will receive payment of $100 for each patient that meets inclusion criteria and is screened within 6 hours of ROSC but is not enrolled. **Payment will be made quarterly** for patients entered in WebDCU as a screen failure by the site.

- The total amount of reimbursements for a single subject shall not exceed **$11,150 (inclusive of F&A costs).** Procedures, timelines and specific information can be found on the trial website, https://siren.network/clinical-trials/picecap

- SIREN SOP for Participant Reimbursement applies. SIREN SOP Participant Reimbursement

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Invoicing

- You see what we see
- Based on contract language
- Subject visit reads READY in WebDCU

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Invoicing

- Invoice creation is not automatic
- We generate the invoice for you at least quarterly
- Invoices can be found in WebDCU
- Retrieve and submit your invoice to your Accounts Receivable office to assist with reconciliation

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Invoicing

Data is entered and free of query


WebDCU™ for ICECAP Current
ICECAP
Subject CRF Binder
Study Progress
Data Management
Project Management
Site Management
Central IRB
Clinical Site
Site Status
Readiness Report
Clinical Site Group Member
Site Payment Summary
Site Invoice
Site Invoice Payment
Site Payment
Payment Definition
Site Contact Log
Data Monitoring
Graphic Reports
Project Setup
User Management
Regulatory Document
Toolbox
Emergency Help
Alerts

Page Actions

Payment Status	Status Date	Date First Ready	Amount Invoiced	Invoice ID	Invoiced On
Not Eligible	11-Feb-2021				
Not Eligible	11-Feb-2021				
Not Eligible	11-Feb-2021				
Not Eligible	11-Feb-2021				
Not Eligible	11-Feb-2021				
Not Eligible	11-Feb-2021				
Not Ready	11-Feb-2021				
Not Ready	11-Feb-2021				
Not Ready	11-Feb-2021				
Not Ready	11-Feb-2021				
Ready	11-Feb-2021	10-Feb-2021			
Invoiced	18-Jan-2021	02-Jan-2021	6000	1069	18-Jan-2021
Invoiced	18-Jan-2021	02-Jan-2021	4500	1069	18-Jan-2021
Invoiced	07-Dec-2020	16-Sep-2020	6000	1036	07-Dec-2020
Invoiced	07-Dec-2020	16-Sep-2020	4500	1036	07-Dec-2020
Invoiced	07-Dec-2020	30-Oct-2020	6000	1036	07-Dec-2020
Invoiced	07-Dec-2020	28-Sep-2020	6000	1036	07-Dec-2020
Invoiced	07-Dec-2020	30-Oct-2020	4500	1036	07-Dec-2020
Invoiced	07-Dec-2020	30-Oct-2020	4500	1036	07-Dec-2020
Invoiced	07-Dec-2020	30-Oct-2020	6000	1036	07-Dec-2020

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Where’s My Agreement?

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Questions?

Contact Teri Behnke @ tbehnke@med.umich.edu

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Regulatory Readiness

Carol Van Huysen

Goals for Today

Provide guidance for navigating the required regulatory processes and be released to enroll as quickly and efficiently as possible

- Steps and order to take them
- Tools and helpful links

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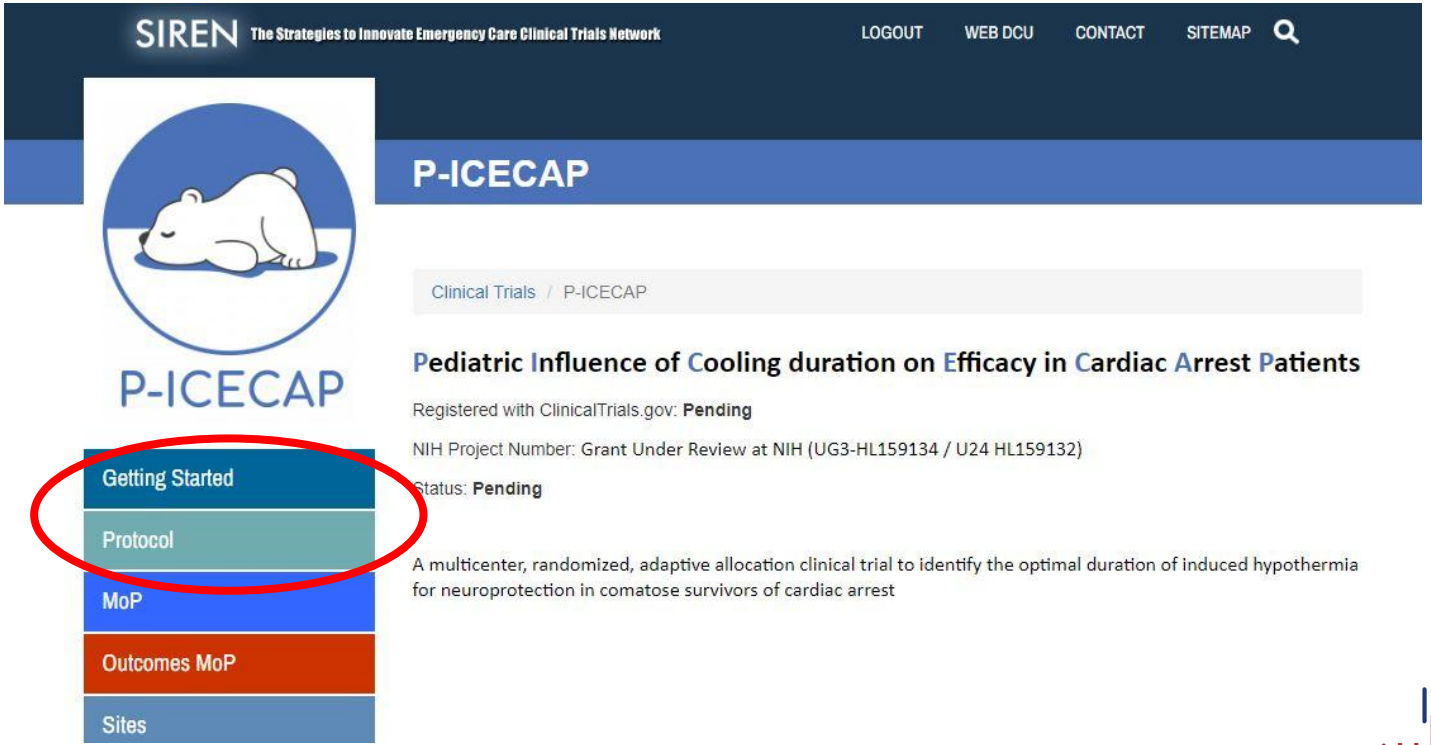
Site IRB cedes to Advarra

Reliance agreements exist between site IRB and Advarra

Site does not have direct contact with Advarra

P-ICECAP Website

https://siren.network/clinical-trials/picecap



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- P-ICECAP regulatory database serves as the central repository for all regulatory documents
- IRB Approvals and other essential documents will be available via the database
- Automated emails will be sent for expired, expiring, and missing documents

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Regulatory Document Approval Parameters

User Management

- Completing the eDOA (electronic Delegation of Authority) Page 2-3

Regulatory Documents

- People Regulatory Document Collection Page 3-5
- Site Regulatory Document Collection Page 6-10

Central IRB (CIRB) Tables

- Step 1: SITE Overview Page 11-13
- Step 2: Site Regulatory Inspection History Page 13
- Step 3: Initial Site Submission - P-ICECAP Database Page 14-35

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Electronic Delegation of Authority Log

The eDOA must be completed by the Primary Study Coordinator

Obtain a UM Friends Account – See Getting Started on website

Request a WebDCU database login at picecap-contact@umich.edu

Enter the research team on the eDOA in WebDCU using the detailed instructions in the Regulatory Parameters document.

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Regulatory Document Approval Parameters

People Document: Specific to an individual study team member

People Document Collection

REGULATORY REQUIREMENTS			APPROVAL PARAMETERS			
Document	**Person Role**	**Document Type**	**Effective Date** dd/mmm/yyyy	**Expiration Date** dd/mmm/yyyy	**Waived Y/N**	**Instructions for WebDCU™** Please upload all documents in **pdf** format to WebDCU™.
CV	Hub PI, Hub PM, P.I., Co-I, Primary SC, Secondary SC	People	Use date within document	2 years from source date	No	Required for all site personnel listed on the 1572/DOA log and any other personnel who are directly involved in the study. Document must have a date. Provide source in a pdf attachment.
HSP Certification	Hub PI, Hub PM, P.I., Co-I, Primary SC, Secondary SC, Reg Doc Coordinator	People	Use source (date certification completed)	Site-specific	No	Please follow the local institutional policies for completion and ongoing maintenance of HSP training. If your institution requires re-training and provides an expiration date for the certification, enter this date into WebDCU™ and you will receive a notification as that date nears. Please provide the corresponding HSP Certification for each study team member in a pdf attachment.

Regulatory People Documents Needed for Startup

All Team Members	Role Dependent
Human Subjects Protection	CV
Good Clinical Practice	Medical License
Protocol Training	Data Training
	Regulatory Training
	Investigator Agreement

**Reminder: Please upload all documents as PDFs in WebDCU

Regulatory Document Approval Parameters

Site Document: Applies to an individual site

Site Document Collection

REGULATORY REQUIREMENTS				APPROVAL PARAMETERS	
Document	**Document Type**	**Effective Date** dd/mmm/yyyy	**Expiration Date** dd/mmm/yyyy	**Waived Y/N**	**Instructions for WebDCU™** Please upload all documents in pdf format to WebDCU™
FWA	site	Use source approval date, if a date is not provided, use date uploaded	Required – use source expiration date	No	Provide documentation of a Federal wide Assurance (FWA). Upload a copy of the FWA, pulled from the OHRP website, to WebDCU™. Please see FWA process document in the BOOST 3 Toolbox. Provide source in a pdf attachment.
CLIA	site	Use source	Use source	No	CLIA certification is the only lab certification required. Provide source in a pdf attachment.

Regulatory Site Documents Needed for Startup

FWA for Institution	Ceding Request to Local IRB
HSP Requirements	Ceding Acknowledgement
Attestation of Training	IRB Approval from Advarra *
Conflict of Interest	IRB Approved Consent Form *

* Populated by database by Advarra

A word about consents.....

The approved Informed Consent Form cannot be modified

Required site specific language may be added in the ‘black box’ section of the approved ICF

Provide the language in a Word document to the CCC

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Regulatory Document Approval Parameters

Complete CIRB Tables

Responses in these WebDCU tables enables the CCC to complete and submit your IRB application for you

- Site Overview - SIREN Database
- Site Regulatory Inspection History - SIREN Database
- Initial Site Submission in P-ICECAP database under CIRB

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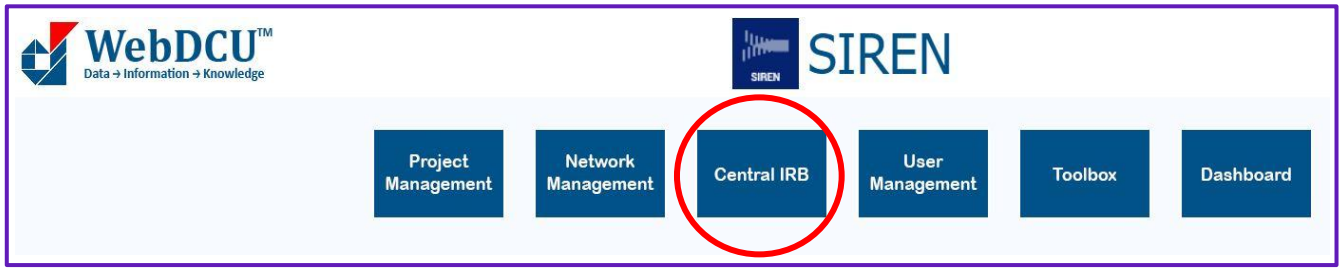

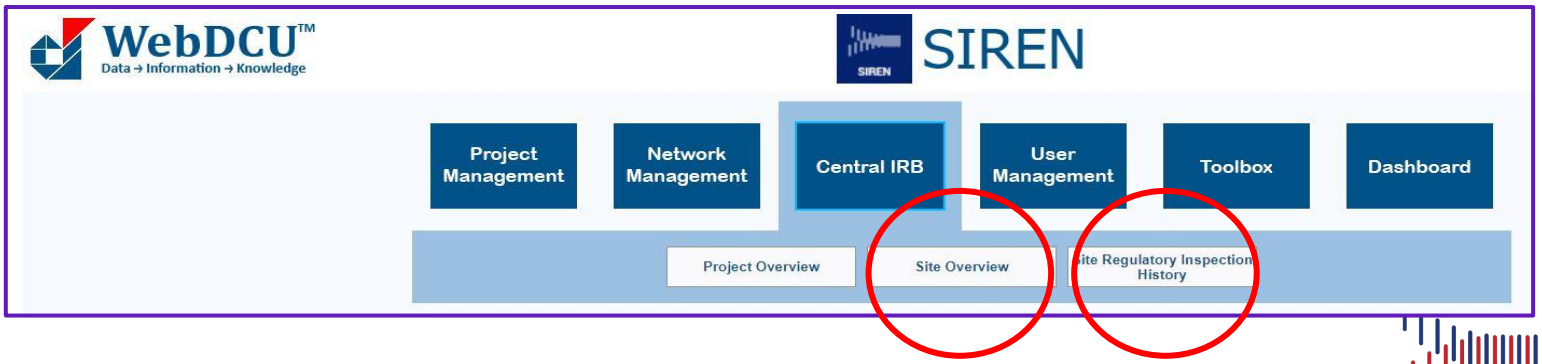

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Complete All Required Training

- Protocol Training: Required for all study team members

  IM Meeting counts!

- Data training: Required for team members responsible for data entry
- Regulatory Document Management Training: Required for Primary Study Coordinators or Regulatory Coordinators if applicable

Training modules will soon be on the Education and Training tab of the website

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Readiness Checklist and Call

- Complete checklist to confirm readiness
- List names of site participants who will attend
- Respond to all questions in logistics section
- Email completed checklist prior to the call
- Request CCC schedule a readiness call

C3PO Readiness Checklist

HUB	
SPOKE/SITE	
DATE OF READINESS CALL	
SITE PARTICIPANTS	Site PI: Site Co-Is: Site Primary Study Coordinator: Hub PI: Hub PM: Other Team Members:
C3PO & SIREN PARTICIPANTS	(For CCC Use) ICECAP PI(s): Dr. Clif Callaway, Dr. Fred Korley SIREN CCC Staff: Carol Van Huysen, Renee Kasperek-Wynn, Valerie Stevenson MUSC Staff: Other:

Contract Status (Check if complete. In incomplete, please explain.)

☐ Pending

☐ Complete

cIRB Tables *(Check if complete. If incomplete, please explain.)*

☐ Site Overview (SIREN > Central IRB)

☐ Site Regulatory Inspection (SIREN > Central IRB)

☐ Initial Site Submission (C3PO > Central IRB)

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Ongoing Site Management

Be Proactive!

- It is the responsibility of each Hub/Site to maintain regulatory compliance, inclusive of site documents and people documents, throughout the duration of the trial
- Documents approaching expiration should be reconciled prior to the expiration date
- Study team personnel who are out of regulatory compliance should not participate in any trial related activities

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Review of Next Steps…

1. Request ceding from IRB
2. Submit eDOA
3. Complete the cIRB tables
4. Follow-up on contract if necessary
5. Start training - frequent reminders to team!
6. Work on orderset
7. Forward site specific language for ICF
8. Upload Site and People documents as received
9. Schedule a readiness call

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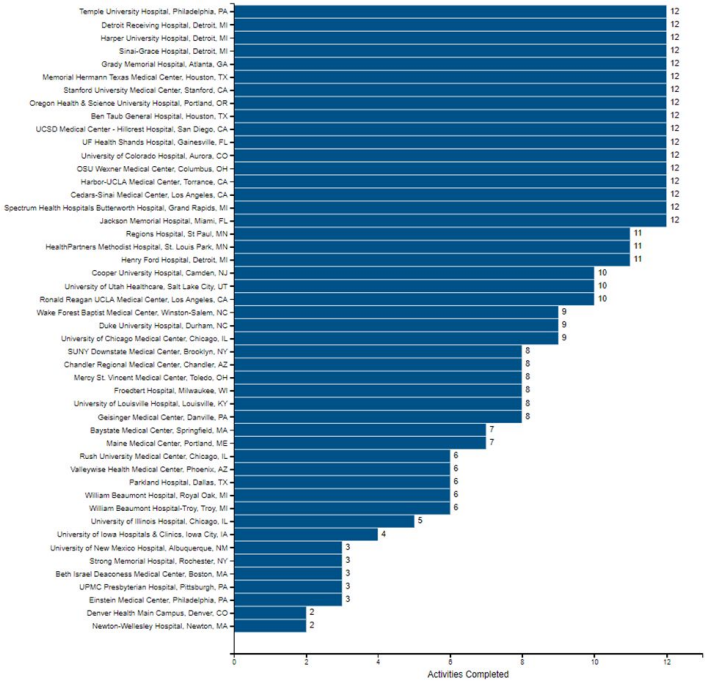
Tracking Readiness in WebDCU



Site Readiness Report

View Progress in the P-ICECAP database under Site Management > Readiness Report

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Join weekly office hours for answers to your questions, or contact us…

picecap-contact@umich.edu

Carol Van Huysen cvanh@umich.edu

Moni Weber monij@umich.edu

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Questions

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Ancillary Study Ideas

Dr. Alexis Topjian

Overview

- Process
- Timing
- Grant Mechanisms
- Idea Brainstorming

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Huge Opportunity

- Largest pediatric post cardiac trial ever
- Anticipated 900 patient to be enrolled over 5 years, 6th year to complete follow up
- Anticipate approximately 50% survival rate approx. 450 survivors

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Process

- Ancillary study ideas will be presented to the Protocol Review Committee of the Executive Committee for their assessments of study feasibility and interest in collaboration.

- EC will review the submitted Grant Proposal

- A letter of support will be provided for grant applications

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Key Considerations

- The proposed study addresses a question of importance.
- The proposed study should not compete with other studies
- Conduct of the study must not adversely affect the parent study.
- Funding will be obtained by the PI and be independent of the parent study.
- Procedures for accessing necessary data and records from the parent study are explicit and acceptable

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Key Considerations

- The proposing PI has the appropriate expertise and facilities to conduct the study.
- Plans for publication and authorship of study results are appropriate, including review and approval of manuscripts per the SIREN publication policy.
- EC members will be given adequate time to review the draft proposal including a draft grant overview before an initial vote is taken.
- 90% approval of the EC is required.

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Key Considerations

- Ancillary studies will not publish before the P-ICEPCAP primary publication

- P-ICECAP data primary data will not be unblinded/revealed for ancillaries

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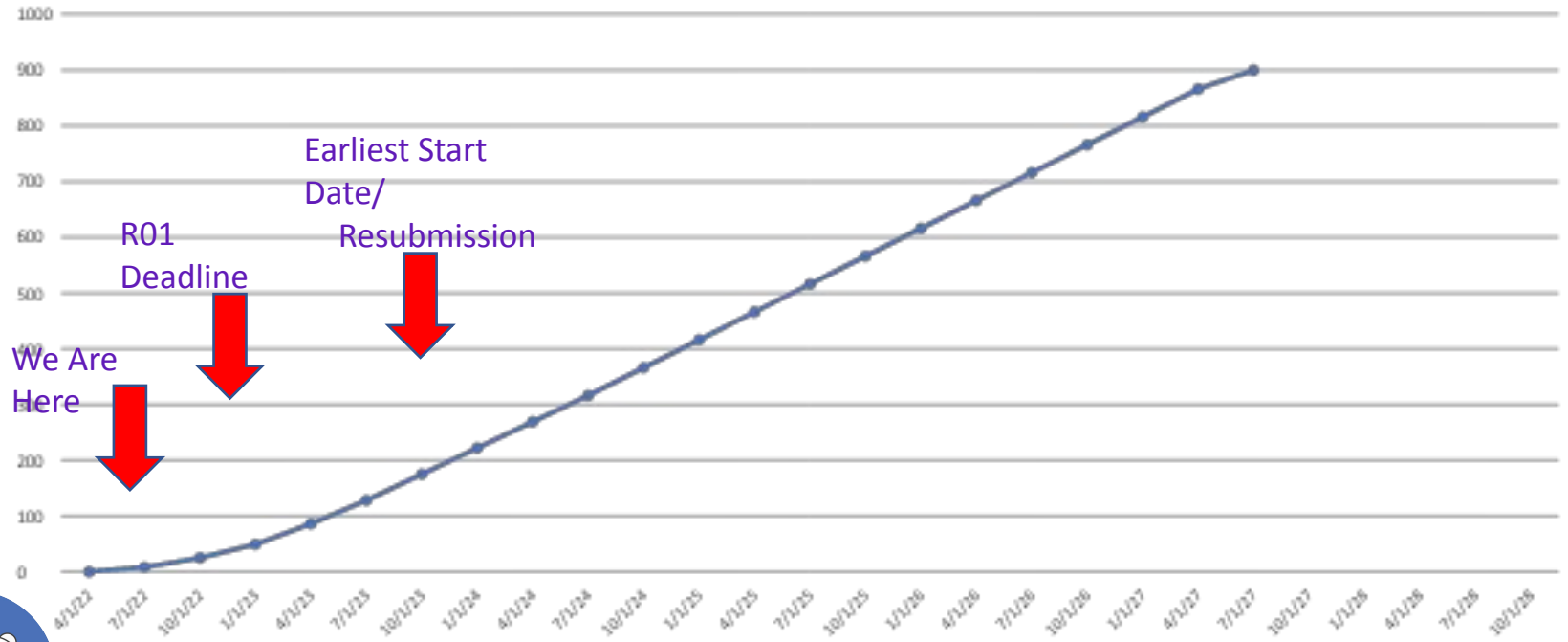
Timeline: PICECAP Anticipated Enrollment



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THAPCA Ancillaries

- Pharmacology of drugs related to cooling. FUNDED
  - Funded but near end of trial

- Effects of cooling on inflammation, immunity NOT FUNDED
  - Not funded but close

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ICECAP Ancillaries

- PREC-ICECAP FUNDED AND ENROLLING
  - Sub phenotyping cardiac arrest injury with EEG and Hemodynamic Data
- COMPACT RESUBMITTED
  - Biomarker Study
- POST-ICECAP PREPARING RESUBMISSION
  - Long Term Outcomes

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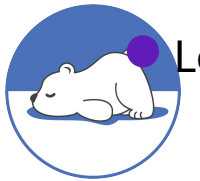
Topics

- EEG monitoring
- Neuroimaging
- Biomarkers
- Inflammation
- Gut microbiome
- Subphenotyping/early injury stratification
- Long Term Outcomes



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Grant Mechanism

- NHLBI R01
- NINDS R01
- American Heart Association
- NIH Diversity Supplement
  - https://grants.nih.gov/grants/guide/pa-files/pa-21-071.html
  - https://www.nhlbi.nih.gov/grants-and-training/training-and-career-development/nhlbi-research-supplement-application-guidelines

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If you are interested.. Next steps

- Email about what you are thinking
- Synthesize your Aims
- Process to submit to the EC will be forthcoming in next couple of weeks

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Survey regarding post arrest care

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Publications

Dr. Frank Moler

Break

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SIREN Website Orientation

Courtney Miller & Carol Van Huysen

Protocol and Standardization Game - Kahoot!

Dr. William Meurer & Moni Weber

Q & A

Drs. Frank Moler, Alexis Topjian, & William Meurer

Thank You and Safe Travels!