CHANGE AFib:

A Pragmatic Randomized Clinical Trial
of Early Dronedarone versus Usual Care to Change and Improve Outcomes in Persons with First-Detected Atrial Fibrillation

Fireside Chat – November 10, 2022

CHANGE AFib is a collaboration between the American Heart Association and the Duke Clinical Research Institute, with support from Sanofi US Services Inc.

Meeting Reminders

Please Note:

- All participants will be muted upon entry.
- Meeting is being recorded and will be archived on our trial website: www.changeafib.org

Questions?

- Please hold questions until our Q&A session at the end of the call.
- Feel free to submit questions in the chat throughout the call, knowing they will be addressed during the Q&A session.

If you are having issue with computer audio, please call in using the appropriate number below.

Dial by your location:

+1 (301) 715-8592	(Washington DC)
+1 (312) 626-6799	(Chicago)
+1 (646) 876-9923	(New York)
+1 (253) 215-8782	(Tacoma)
+1 (346) 248-7799	(Houston)
+1 (669) 900-6833	(San Jose)

Meeting ID: 827 2143 5136
Passcode: changeafib

Agenda:

- Welcome & Introductions
- Trial Progress Update
- Protocol Amendment Review
- Screening & Enrollment Action Items
- Q&A
- Trial Reminders & Closing

Trial Progress Update

Trial Progress – as of November 10, 2022

Site Status	Current Status	Trial GOAL!
Subject Enrollments	**22**	**3000**
Activated Sites	26	**200**
Sites in Onboarding	61	**-**
Sites Assessing Feasibility	38	**-**

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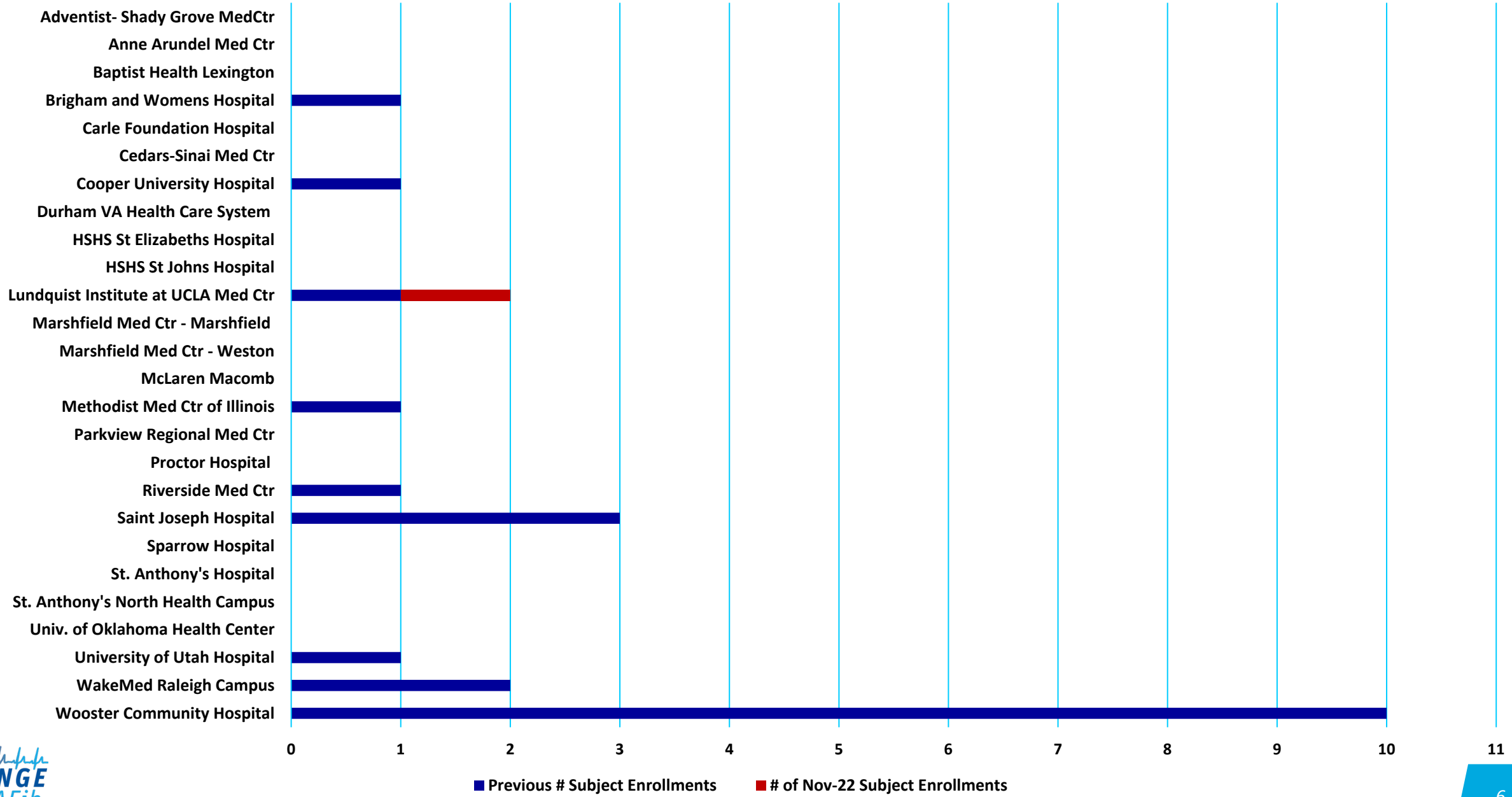
Subject Enrollments by Site (22)



Above data current as of 10Nov2022

Congrats & Thank You to Wooster Community Hospital

Protocol V2.0 Amendment Review

Section 1.2: Schedule of Activities

- Full revision of **"Trial Visit Data Capture Requirements & Schedule"** table. (See Protocol for full details.)
- The table reflects the **collection of data** that is being conducted **during** the patient's clinical care.
- This is a **pragmatic trial** and, consistent with the design, there are **no** diagnostic procedures or laboratory studies **required by the protocol.**
- All of the **data recorded** are **data captured** in the course of the **patient's clinical care.**

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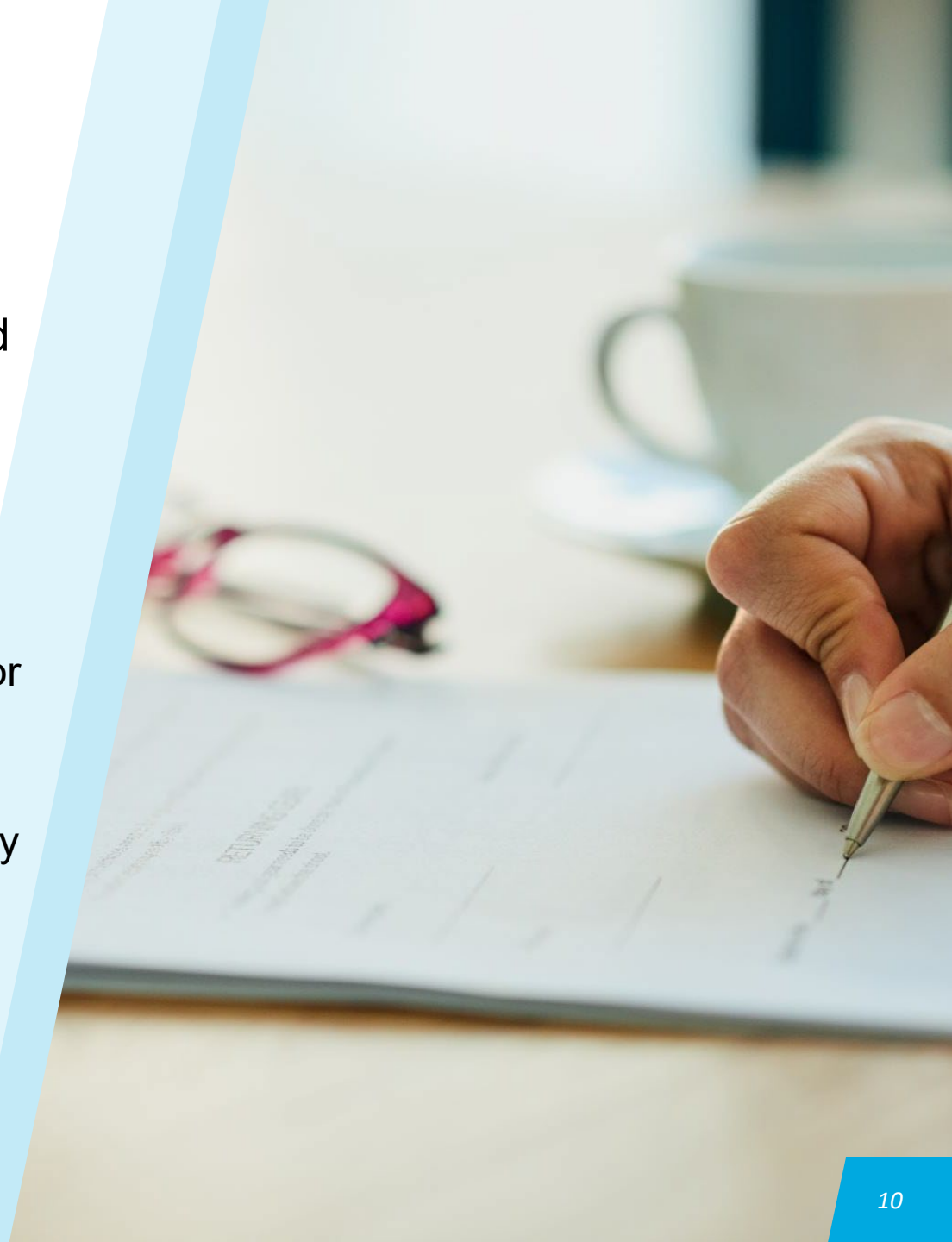
Section 5.1: Inclusion Criteria

- **Age** lowered from 60 to **21 years or older.**
- **Definition of first-detected Atrial Fibrillation** extended from diagnosis in previous 60 days to **120 days**.
- **Acute care encounter** defined as the evaluation or treatment of atrial fibrillation within 120 days.
  - Further clarified that patients can be enrolled from the *inpatient setting* during this qualifying acute care encounter or afterwards in the *outpatient setting*, so long as the qualifying acute care event has occurred in the past 120 days.
  - Acute care encounters are defined as a visit to an emergency department, observation unit, or hospital admission.
- Eligibility of consent by **Legally Authorized Representatives**



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Section 5.2: Exclusion Criteria

- Clarification on definition of **chronic antiarrhythmic drug therapy** (defined as **> 7 days** of treatment).
- Clarification of **prior hospitalization for AF** to explicitly not include the qualifying first-detected AF acute care encounter event.
- Expansion of criteria #11 to exclude **patients currently breast feeding.**
- Clarification of criteria #12 to **defer to the opinion of the investigator** on constitution of **severe hepatic impairment.**

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Section 6.2:
Study Intervention Compliance

- Clarification on **study intervention start time**.
  - Participants in the **intervention arm** will be contacted **within 10 days of randomization** to verify that they have **filled and started taking their prescription** for dronedarone.

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Section 6.3: Concomitant Treatment

- Addition of the following:
  - **Cardioversion** (pharmacologic or electrical) is **not an exclusion** and **is permitted throughout the trial**.
  - Patients who are **planned or scheduled to undergo catheter ablation** during screening or at the baseline visit **are not eligible**.
  - **Following enrollment**, if a patient experiences escalation of symptoms or refractory symptoms, **escalation of rhythm control interventions, including catheter ablation, can be considered if deemed necessary by the patient's treating physician.**

- **Antiarrhythmic Drug Therapy** Definition Added
  - Orally administered **antiarrhythmic drugs** for the treatment of atrial fibrillation **include Vaughan-Williams class I and III medications**, including flecainide, propafenone, sotalol, dofetilide, dronedarone, and amiodarone. Note, beta-blockers (class II) and non-dihydropyridine calcium channel blockers (class IV) are not membrane active antiarrhythmic medications.

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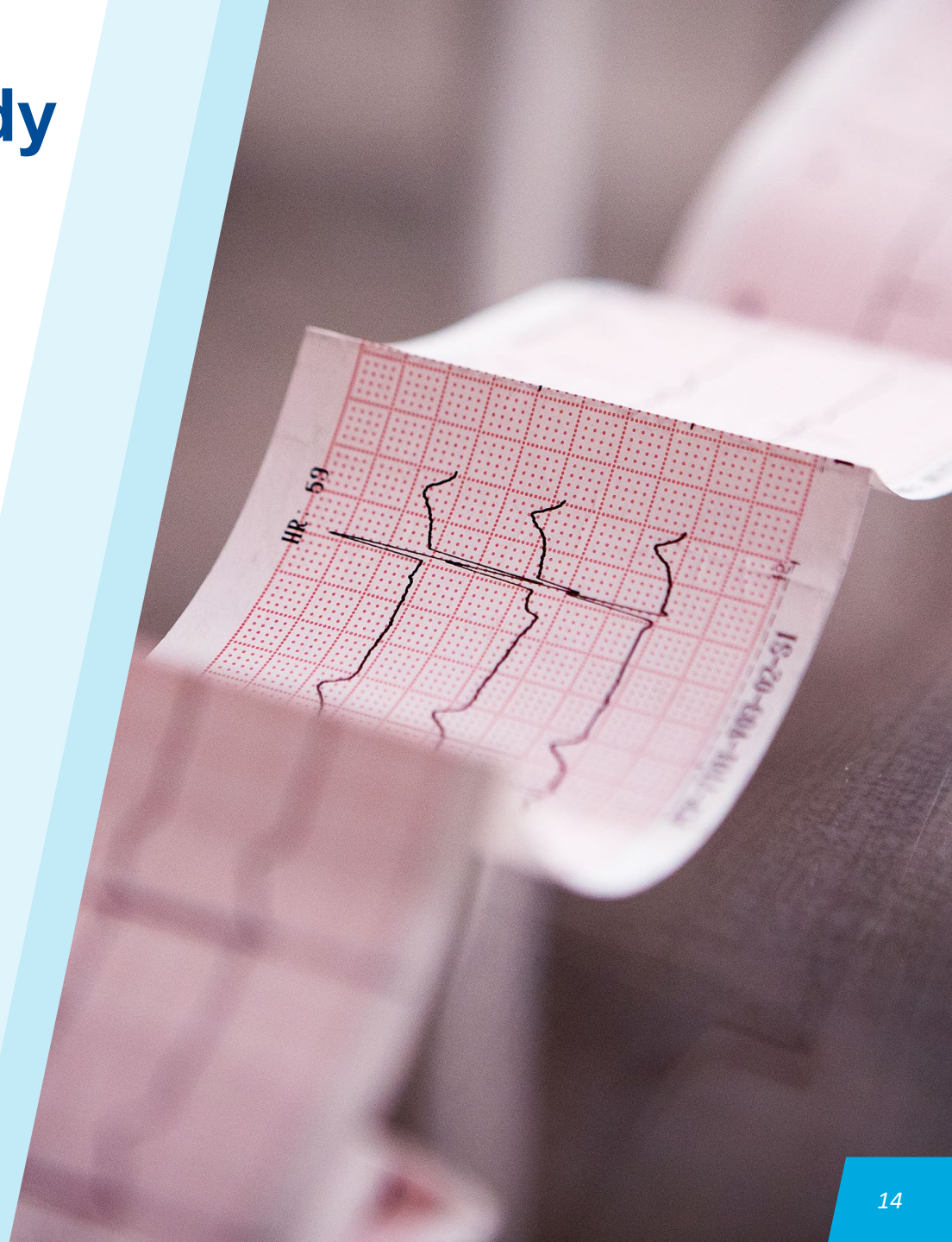
Section 7: Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal

- Additional clarification provided indicating that **patients should not be discontinued** when they experience a **primary endpoint event.**
- Patients should **continue** in the trial **until the end of study visit** at the end of follow-up.
- The **study intervention** therapy should be **continued** unless deemed otherwise by the treating physician or if the patient requires initiation of a different antiarrhythmic medication.



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Section 8: Study Assessments and Procedures

- Additional clarification provided indicating that patients **can be enrolled** in the **inpatient setting** during their qualifying **acute care encounter** or afterwards in the **outpatient setting** so long as their new-onset atrial fibrillation and acute care visit were in the **prior 120 days**.

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Section 8.1: Pregnancy

- Revision as follows:
  - Women of reproductive age should use measures to **prevent pregnancy during the study**… **Pregnancy** will be recorded as an **adverse event** in all cases and **dronedarone should be immediately discontinued**.
- Removal of specific birth control methods, as intervention arm subjects should **follow the package insert** as the **study medication is FDA approved**.

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Next Steps for IRB

Central IRB Sites

- All Central IRB sites were reviewed and approved for Protocol V2.0 (dated 17Oct2022) immediately following the Master IRB Approval.
  - Date of Master IRB Approval: 24Oct2022
  - Date of Master IRB Approval Notice: 31Oct2022
  - Date of Initial Protocol V2.0 ICF: 24Oct2022
  - Date of FINAL Protocol V2.0 ICF: 04Nov2022
- **If your site requires a translated ICF, please reach out to your assigned AHA Site Manager or CHANGEAFibContracting@heart.org**
- Due to a minor ICF typo caught after IRB approval, multiple IRB approval emails were sent out to all Central IRB sites.
- Site-specific IRB Approval notices and ICFs are currently being sent individually to each site- **see subsequent slide for list of sites approved to enroll under Protocol V2.0**

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Next Steps for IRB

Local IRB Sites

- All IRB approved documents to support your local submission have been posted on the trial website **HERE**.
- **Please send any ICF edits to CHANGEAFibContracting@heart.org for sponsor approval prior to Local IRB submission.**
- Upon receipt of sponsor approval, please proceed with Local IRB submission and inform your AHA Site Manager of your site's expected timeline for IRB approval.
- ***Until your site receives Local IRB approval, you are only able to enroll CHANGE AFib subjects under Protocol V1.0 eligibility criteria.***

DCRI REDCap Study Shell

Platform for Eligibility Criteria, Consent & Randomization

- **REDCap Study Shell Update:**
  - The DCRI team is currently updating all CHANGE AFib REDCap study shells to reflect Protocol V2.0.
  - If your site is activated or soon-to-be activated, you should've already heard from the DCRI team regarding "downtime" in your REDCap study shell to accommodate the programming.
  - Formal Enrollment Approval notifications are being sent to all sites when all updates are complete.
  - Reach out to your AHA Site Manager with any questions!
- **eConsent ON HOLD:**
  - If your site is utilizing the sponsor-provided eConsent platform within REDCap, you will receive a formal notification when your new ICF has been uploaded into your site's REDCap portal.

As of 10Nov2022- Sites Approved to Enroll Under Protocol V2.0

(IRB Approved & REDCap Study Shell Update Complete)

- Adventist HC Shady Grove Med Center
- Brigham and Women's Hospital
- Cooper University Hospital
- Lundquist Institute (UCLA Medical Center – Harbor)
- HSHS St Elizabeth's Hospital – Prairie Health
- HSHS St. John's Hospital – Prairie Health
- Luminis Health Anne Arundel Medical Center
- Marshfield Medical Center - Marshfield
- Marshfield Medical Center - Weston
- McLaren Macomb
- MetroHealth Medical Center
- Parkview Regional Medical Center
- St. Anthony Hospital (Colorado Heart and Vascular)
- St. Anthony Hospital North Health Campus (Colorado Heart and Vascular)
- Wooster Community Hospital

All sites will receive a formal enrollment approval email with the updated screening log template.

List of Updated Documents

All Protocol V2.0 documents are posted on CHANGEAFib.org

- Main Study IRB Approval (31OCT2022) – HERE
- Protocol V2.0 –17OCT2022 – HERE
- Summary of Changes, Protocol V2.0 – 17OCT2022 – HERE
- Protocol V2.0 ICF Template – HERE
- Protocol V2.0 ICF Template_Tracked Changes – HERE

Coming Soon:

- **Recruitment Materials** – Trial Brochure & Provider Pocket Cards are currently under production and will be distributed & posted to the trial website shortly!

- **Updated Protocol V2.0 Screening Log** – Included in formal enrollment approval notification to sites from AHA CHANGE AFib team.

Summary of Next Steps

1. **Protocol V2.0 Site Training**
   - Establish focused time with CHANGE AFib trial team to thoroughly review Protocol V2.0 and Summary of Changes
   - Principal Investigator sign & submit Protocol V2.0 Signature Page
2. **IRB Approvals**
   - Central IRB Approval Emails with notification & ICFs.
   - Local IRB sites to submit ICF changes needed prior to IRB submission.
   - Please make sure to file all documents according to site/institution requirements.
3. **REDCap Site Updates**
   - Protocol V2.0 Enrollment Approval Emails
   - eConsent on HOLD for now – Stay tuned for updates!
4. **Screening & Enrollment**
   - **START** Screening for Protocol V2.0 eligibility criteria using the update Screening Log (V5_07Nov2022)!
   - **ENROLL** 2 subjects a week to help us get to the **2022 Year End GOAL!**

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Subject Enrollment Action Items

TRIAL ENROLLMENT GOAL

2022 YEAR END GOAL:

300 SUBJECTS

2 SUBJECTS PER SITE PER WEEK

Our year-end goal can be achieved if all sites enroll at least 2-subjects per week!

As we are consistently activating new trial sites, we know can meet this 2022 goal together!!

Screening & Enrollment Requirements for Success

Tasks by End of Year 2022

- Screening Strategies
  - Manual Screening vs EMR Report reviews
  - Daily review of patients currently in ER or on cardiology floors/services
  - Daily collaboration with outpatient clinics and schedules for potential patients
  - Retroactive review of previously submitted screening logs due to increased diagnosis window (120-days)
    - Review diagnosis dates of subjects previously ineligible due to Protocol V1.0 60-day diagnosis window.
    - Review subjects previously listed as ‘planned for OP enrollment’
- Trial Visibility throughout the Site
  - Promote CHANGE AFib at routine departmental meetings or grand rounds
  - Identify a trial champion in various areas of your site (ER, OP clinics, etc.) & circulate provider pocket cards!

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Q&A

Trial Reminders

Mark Your Calendars!

Upcoming Fireside Chats

- **Monday, December 12th, 12-1pm ET** **Next Up**

2023 Dates to be Announced Shortly!

**Archived webinar recordings & handouts can be found HERE on the trial website.*

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Connect With Us!

How to reach the CHANGE AFib Team

AHA Site Managers:

Crystal.Glodek@heart.org

Jack.Goldberg@heart.org

Mariel.Dronson@heart.org

ChangeAFib@heart.org

Resources to Remember

For important trial information and today's meeting recording, go to the **Resources** page at **www.changeafib.org** or visit the QR Code to the left.