

# Developing the Safety of Atrial Fibrillation Ablation Registry Initiative (SAFARI) as a collaborative pan-stakeholder critical path registry model: A Cardiac Safety Research Consortium “Incubator” Think Tank

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Although several randomized clinical trials have demonstrated the safety and efficacy of catheter ablation of atrial fibrillation (AF) in experienced centers, the outcomes of this procedure in routine clinical practice and in patients with persistent and long-standing persistent AF remain uncertain. Brisk adoption of this therapy by physicians with diverse training and experience highlights potential concerns regarding the safety and effectiveness of this procedure. Some of these concerns could be addressed by a national registry of AF ablation procedures such as the Safety of Atrial Fibrillation Ablation Registry Initiative that was initially proposed at a Cardiac Safety Research Consortium Think Tank meeting in April 2009. In January 2010, the Cardiac Safety Research Consortium, in collaboration with the Duke Clinical Research Institute, the US Food and Drug Administration, the American College of Cardiology, and the Heart Rhythm Society, held a follow-up meeting of experts in the field to review the construct and progress to date. Other participants included the National Heart, Lung, and Blood Institute; the Centers for Medicare and Medicaid Services; the Agency for Healthcare Research and Quality; the AdvaMed AF working group; and additional industry representatives. This article summarizes the discussions that occurred at the meeting of the state of the Safety of Atrial Fibrillation Ablation Registry Initiative, the identification of a clear pathway for its implementation, and the exploration of solutions to potential issues in the execution of this registry. (Am Heart J 2010;160:619-626.e1.)

Pulmonary vein isolation using percutaneous catheter ablation of atrial fibrillation (AF) is expanding rapidly. Although this procedure has been demonstrated in several randomized clinical trials (RCTs) to reduce the risk of recurrent AF, these trials were limited by the relatively small sample size, the limited follow-up period of  $\leq 1$  year, the very experienced operators performing the procedure,

the highly selected patients who were relatively young and who had no or mild structural heart disease, and the highly variable monitoring for recurrent AF during follow-up.<sup>1-11</sup> Some of these limitations will be addressed by the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA), a National Heart, Lung, and Blood Institute (NHLBI)-funded multicenter RCT of

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<sup>p</sup>For an expert panel participating in this meeting. See online Appendix A for complete listing. An educational collaboration among the CSRC, DCR, ACC, HRS, AdvaMed, and US FDA. This conference was funded by the CSRC, DCRI, ACC, HRS; registration fees and in-kind support from the FDA and AdvaMed. Submitted June 22, 2010; accepted June 22, 2010. Reprint requests: Sana M. Al-Khatib, MD, MHS, Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715. E-mail: [alkha001@mc.duke.edu](mailto:alkha001@mc.duke.edu) 0002-8703/\$ - see front matter © 2010, Mosby, Inc. All rights reserved. doi:10.1016/j.ahj.2010.06.044

catheter ablation versus pharmacologic therapy for symptomatic AF (NCT00911508).<sup>12</sup> However, CABANA, like any other RCT, will provide only limited data on the techniques, safety, and durability of the effect of this procedure in routine clinical practice. Furthermore, in a rapidly changing landscape of imaging and monitoring systems, ablation catheters, and new antiarrhythmic and antithrombotic therapies, by the time more RCT results are reported, there will inevitably be new questions relevant to current practice.

Recognizing the need for an ongoing portal to informative data, the Cardiac Safety Research Consortium (CSRC) organized a pan-stakeholder Think Tank meeting on April 27-28, 2009, at the US Food and Drug Administration (FDA) headquarters in Silver Spring, MD, to consider the development of a national registry, the Safety of Atrial Fibrillation Ablation Registry Initiative (SAFARI). As previously reported, there was consensus among most meeting participants that SAFARI would be a useful infrastructure to collect important information on the safety and potentially on the effectiveness and durability of AF ablation in routine clinical practice.<sup>13</sup>

As a follow-up to that meeting and to continue the development of SAFARI, the CSRC, in collaboration with the Duke Clinical Research Institute (DCRI), the American College of Cardiology (ACC), the Heart Rhythm Society (HRS), the NHLBI, the FDA, the Centers for Medicare and Medicaid Services (CMS), the Agency for Healthcare Research and Quality (AHRQ), AdvaMed, and additional device and pharmaceutical industry representatives, conducted a second "Incubator" Think Tank meeting on January 13, 2010, at the Seaport Conference Center, Boston, MA, preceding the 15th Annual Boston AF symposium. The specific objectives of the meeting were to (1) discuss the state of SAFARI development since the previous meeting, (2) revisit the objectives and construct of SAFARI, and (3) identify current barriers and explore solutions related to the timely and pragmatic execution of this registry. The names and affiliations of all participants in this second meeting are listed in the online [Appendix A](#).

## An update on SAFARI

Since the meeting in April 2009, several steps in the development of this registry have been completed. First, an executive committee has been formed; and a steering committee is being formed. Second, a charter for SAFARI has been drafted detailing the mission of the registry, the objectives of the SAFARI collaboration, the governance structure of the registry including roles and responsibilities of the different parties, and a plan for its implementation. Third, data collection forms for SAFARI have been developed and beta-tested in conjunction with the ACC-National Cardiovascular Data Registry (NCDR).

As drafted, the mission of SAFARI is to facilitate a national pan-stakeholder collaboration supporting the design, implementation, and maintenance of a logistically feasible registry platform for systematic data collection characterizing the safety and possibly effectiveness and durability of on- and off-label "real-world" AF ablation.

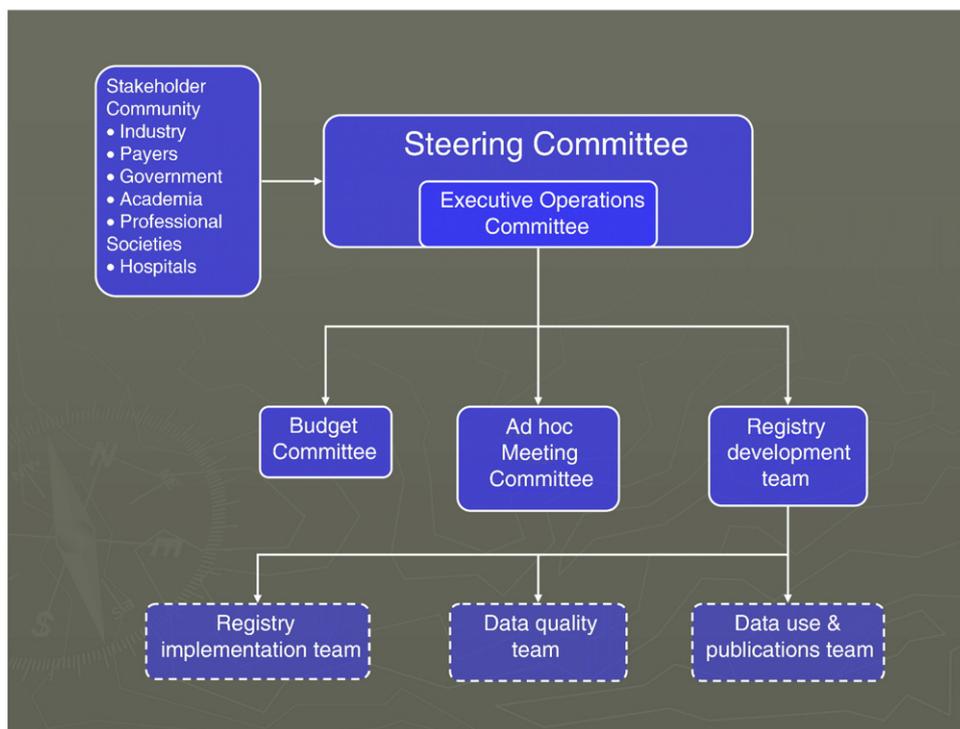
The drafted objectives of SAFARI are (1) to establish a transparent, nationwide registry for collecting data related to AF ablation and (2) to report the data contained in the registry. Specifically, SAFARI will (1) continue to develop a framework for collaborative participation of multiple stakeholders through its administrative infrastructure, (2) support synergistic and collaborative efforts to bridge the knowledge gaps that exist in the field of AF ablation, (3) ensure that information resulting from these collaborative efforts is appropriately disseminated to the medical community and the public, (4) inform regulatory decision making as appropriate, and (5) inform related activities including clinical trials and professional society guidelines on the application of ablative therapies for AF.

Partners in SAFARI include the FDA, the CSRC, the ACC-NCDR, the HRS, and the device and ablation catheter manufacturing industry. The current draft of SAFARI's governance structure is shown in [Figure 1](#).

The implementation of SAFARI is proposed over several phases. Phase 0 is the current planning phase aimed at establishing the purpose and the scope of the registry, identifying the full range of stakeholders, establishing working groups and committees to focus on various aspects of the registry, determining the governance and management of the registry including data management and analysis plans, addressing regulatory and legal issues in implementing the registry, and securing funding. In phase 1, a pilot roll-out of SAFARI will be completed and carefully evaluated. Phase 2 is proposed as an implementation phase that involves new site training, patient enrollment, monitoring of data quality, and assessing when registry implementation has been achieved. Phase 3 involves data analysis based on a prospective statistical analysis plan and communication of results via peer-reviewed publications. With the rapid evolution of AF ablation, these phases will have to adapt to changing circumstances and new developments in the field.

Three data collection forms for SAFARI have been developed and beta-tested: a long baseline and index procedure case report form (CRF) (intended for a select number of sites), a short baseline CRF (intended for all sites), and a follow-up form. The results of the beta-testing were presented at the meeting. Nine sites participated by collecting data on all catheter ablations for AF occurring from December 1 through December 15, 2009. Most sites completed the CRFs; however, the forms were felt to be burdensome to complete and in need of more understandable and concise definitions. Some procedural information was not readily available from medical records. Several aspects of the follow-up form also

**Figure 1**



The governance structure of SAFARI.

needed clarification including timing and information on the logistics of collecting data from referring facilities not performing the index procedure. Based on these discussions, a plan was formulated to obtain further feedback from participants in the second SAFARI Think Tank meeting and have the CRF working group revise the forms accordingly before proceeding to the pilot study.

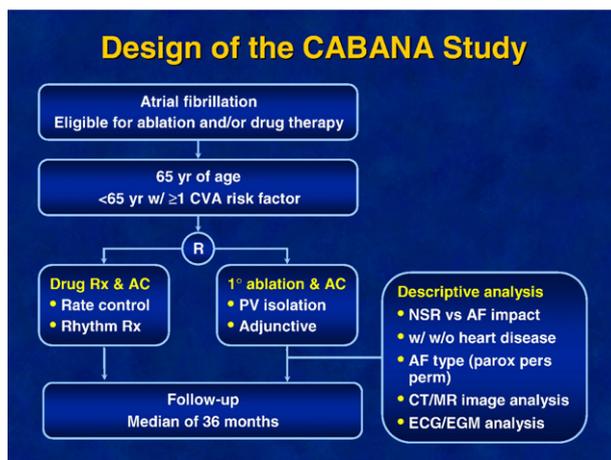
Whether SAFARI could proceed as an observational database, similar to the current ACC-NCDR registries, or whether it would require an investigational device exemption (IDE) was extensively discussed. The FDA representatives from the Center for Devices and Radiologic Health suggested that an IDE may be necessary because SAFARI involves the use of devices that have risk and most of these devices are not yet approved for AF ablation. Proceeding with an IDE might also address industry's concern regarding the regulatory perception that participation in this registry might be construed as promoting off-label products given that compliance with the IDE regulation means that devices are not being promoted as safe and effective. The FDA representatives emphasized that an IDE submission would need to address the requirements of 21 CFR 812, listing all devices to be included in SAFARI, specifying a maximum number of patients to be enrolled, and explaining how the study data will be accessed. If SAFARI is conducted under an IDE, manufacturers would need to grant a

written right of reference to premarket applications. As new technologies become available, they could be added to the IDE submission via a supplement. The FDA representatives also indicated that, for an IDE, there might be a need to obtain the approval of each institutional review board and the consent of patients both for the procedure as well as for the data that are being collected. Finally, the Center for Devices and Radiologic Health representatives recommended that a data quality committee meet periodically to randomly sample data quality and that a data and safety monitoring board meet regularly to monitor safety end points.

Many participants in the meeting voiced strong concerns over the impact of requiring an IDE and an investigational consent on the workload of sites and enrollment rates. Specifically, the need for obtaining informed consent has the potential to dramatically limit the widespread enrollment of patients in the registry. The FDA has committed to providing additional guidance regarding the scenarios for which an IDE is required. If an IDE is needed, the FDA will provide advice to the sponsor of the SAFARI IDE on how to execute an IDE that complies with all regulatory requirements while not undermining the goals of SAFARI.

Two projects that could inform SAFARI's activities were presented at the meeting, namely, the Medicare Evidence Development and Coverage Advisory Committee meeting

Figure 2



The design of the CABANA trial.

held on October 21, 2009, and the CABANA trial. Although the Medicare Evidence Development and Coverage Advisory Committee meeting concluded that catheter ablation is an effective second-line therapy for paroxysmal AF (it reduces recurrent AF and improves patient symptoms), it highlighted several uncertainties about this procedure including the lack of data on the effect of the procedure on stroke risk and death, the effectiveness of catheter ablation for long-standing persistent AF, the potential role of AF ablation as first-line therapy or as a therapy for first detected AF, long-term (>1 year) outcomes, and whether outcomes can be extrapolated to patients outside a controlled clinical trial and to the Medicare beneficiary population ( $\geq 65$  years, 56% female).<sup>14</sup> These uncertainties highlight the importance of SAFARI and the CABANA trial.

The CABANA trial is a multicenter RCT comparing catheter ablation with pharmacologic therapy for symptomatic AF. The design of the trial is shown in Figure 2. This trial, which started enrolling patients at the end of 2009, is expected to address some of the current uncertainties about catheter ablation for AF.<sup>12</sup> The main differences between CABANA and SAFARI are shown in Table I. It is hoped that the prospective designs of CABANA and SAFARI will not only complement each other, but could also become synergistic and mutually informative. To support this plan, similar data elements and identical data definitions for CRFs are being used in both studies.

### Questions to be addressed by SAFARI

Several aspects of AF catheter ablation are considered well established. First, this therapy appears to be more

Table I. CABANA versus SAFARI

	CABANA	SAFARI
Treatment assignment	Randomized	Individual preference
Treatment comparisons	Designed-specified	Pre and post hoc
Sample size	3000 patients	$\geq 5000$ patients
Hypothesis	Confirming	Generating
Challenges	Enrollment and retention	Consistency, data quality, collecting long-term follow-up data, enrolling the majority of patients who undergo an AF ablation in the United States
Trial funding	NIH and industry	To be determined
Applicability	Ideal world (specific population)	Real world (broad population)
Scope	International	Limited to the United States

effective than antiarrhythmic medications at reducing drug-refractory, symptomatic AF in middle-aged patients with paroxysmal or persistent AF at 12 months of follow-up when the ablation is performed by experienced operators. Second, this procedure has the potential to improve patients' quality of life. Third, when performed by experienced operators, catheter ablation of AF is associated with a 2% to 5% risk of serious complications.<sup>1-11</sup>

Despite these findings, much remains to be learned about AF catheter ablation. First, the safety and effectiveness of this procedure in a wider variety of clinical settings (academic, nonacademic, low- and high-volume centers) need to be examined. Second, the effect of low-volume operators on patient outcomes should be explored. Third, the safety and effectiveness of this procedure in older patients, patients with heart failure and other comorbidities, and patients with long-standing persistent AF need to be investigated. Fourth, whether catheter ablation is effective as first-line therapy for AF needs to be studied. Fifth, more information is needed on the long-term effectiveness and safety (>12 months) of this procedure including the optimal use of adjunctive antiarrhythmic and antithrombotic medications. Sixth, several questions need to be answered in relation to the optimal ablation strategy; the role of linear lesions and ablation at sites with complex fractionated atrial electrograms and non-pulmonary vein sites (eg, superior vena cava and coronary sinus); different ablation tools; imaging techniques before, during, and after ablation; and ablation end points. Finally, more general data are needed on how many AF ablation procedures are being performed each year, what patients are undergoing AF ablation, what operators and hospitals are performing this procedure, and how many patients require repeat AF ablation procedures.

Many of these questions could potentially be addressed by SAFARI as an ongoing registry; however, it is also

important to recognize that not all questions can be addressed by a registry design. For example, the most definitive data on the impact of AF ablation on stroke risk and death relative to other treatment strategies may be best obtained in the context of a multicenter RCT. Questions related to the effectiveness of AF ablation can be best addressed if a common definition of *success* is used, if careful and consistent follow-up and electrocardiographic monitoring are performed, and if methods of monitoring data quality and accuracy are well established. It is recognized that incorporating such effectiveness end points, an integral part of RCTs of AF ablation, may pose additional financial and administrative burdens on participating centers and the registry as a whole. Although such effectiveness end points may not be the initial objective of the SAFARI registry, most of the participants in the meeting agreed that data on safety can only be meaningfully interpreted if data on effectiveness are also available.

Notwithstanding the intrinsic limitations of a registry format, SAFARI was broadly recognized as an infrastructure that can aid in quality improvement, benchmarking, quality measures, and postmarket product surveillance. It can thus inform utilization of practice guidelines and consensus, and it can support the evolution of “real-world” AF ablation therapy.

## Phasing of registry implementation

The implementation of SAFARI will be conducted in 4 phases. Phase 0 is a planning phase that is currently under way. To complete this phase, the following steps have been taken. The purpose and scope of SAFARI have been drafted, the questions that SAFARI will address are being refined, multiple stakeholders have been engaged, and several working groups or committees have been established. An executive committee to which all committees other than the steering committee will report has been formed. A steering committee of representative stakeholders is being formed to guide the executive committee. A plan for data collection, management, and analysis is being developed; and regulatory and legal issues involved in implementing the registry are being addressed.

Participants in the meeting agreed that a pilot study is the most efficient and pragmatic step to launch SAFARI. This pilot study will constitute phase 1. The main purpose of the pilot is to test the data collection process and make any necessary changes to the CRFs. Although a consensus objective of SAFARI is to collect data from a wide range of clinical centers, it was generally agreed that limiting the pilot study to the more experienced practices would be best because it would expedite implementation of the pilot study. The pilot study could allow assessment of compliance with procedural and follow-up data capture. Many participants emphasized the importance of collect-

ing follow-up data in the pilot study. This would allow evaluation of different follow-up data collection methods and modifications to address specific questions related to both short- and long-term safety and effectiveness.

As proposed, phase 2 involves training a wider range of sites in data collection, patient recruitment, and data monitoring, and determining when registry completion criteria are met. Criteria for successful data completion should be defined prospectively. The group agreed that collecting follow-up data is essential for the success of SAFARI; however, everyone acknowledged the many challenges involved in this process. How much follow-up is needed and over what period were discussed. Some called for 5 years of follow-up, and others argued that data collection should continue until the registry is no longer relevant. There was general consensus that the duration of follow-up should be specified at the inception of the registry because adding follow-up requirements at a later stage may be difficult. Several additional logistical decisions about collecting follow-up data need to be made before the inception of the registry. These decisions involve whether data collection will be centralized versus localized, how follow-up data will be gathered (clinic visits, telephone contact, mailed questionnaires, etc), and whether some follow-up data will be collected by linking the registry to administrative data such as outcomes (death, stroke, hospitalizations) from Medicare Claims data.

Whether SAFARI will continue to collect data indefinitely was also discussed. Ordinary reasons to stop a clinical trial are the very reasons why a registry like SAFARI should continue as long as the procedure is still being performed in clinical practice. Although the majority of participants in the meeting agreed that stopping rules that may apply to RCTs do not apply to SAFARI, they emphasized the need to reevaluate the costs and value of the registry at regular intervals. Others expressed the view that good clinical research practice dictates stopping data collection once prespecified questions have been adequately answered. Such milestones may be particularly useful to ensure that data are analyzed and reported in a timely fashion. Using embedded specific and prospective hypotheses within SAFARI was discussed as a means to potentially support such reporting while continuing to accrue new information. Participants in the meeting generally agreed that there should be flexibility in the registry that can accommodate evolving technologies and emerging safety and effectiveness questions. It will be important to establish an independent committee whose task is to update the data collection process by keeping the registry current and relevant to practitioners and assess the costs and benefits of its continuation.

Phase 3 involves analysis of data using a prospective statistical analysis plan and dissemination of results via peer-reviewed publications. A more detailed

discussion of phase 3 is planned once phases 0 and 1 are more developed.

## Funding issues/opportunities for registry development

Determining the funding mechanism for SAFARI is critical to the quality and success of this registry. Funds are needed for managing committees, accounts and contracts, recruiting patients, marketing, providing clinical support, orientation and training, and developing data collection tools (data set, CRFs, or Web-based data collection tools, etc). Funds are also needed for collecting data, measuring and monitoring data quality, managing information, providing timely reports to sites, analyzing data, disseminating results, and linking the registry with other databases where applicable. How much funding is required is directly related to the magnitude and quality of data collection required for SAFARI's objectives and to the length and extent of data collection in follow-up.

Prior registries have been either voluntary (Society of Thoracic Surgeons and the ACC-NCDR CathPCI Registry) or linked to reimbursement (Implantable Cardioverter Defibrillator [ICD] Registry and Carotid Artery Revascularization and Endarterectomy Registry).<sup>15-17</sup> Funding for the Longitudinal ICD Registry is being provided by the NHLBI, AHRQ, and industry.<sup>15</sup> The Interagency Registry for Mechanically Assisted Circulatory Support was launched as a joint effort of the NHLBI, the CMS, the FDA, physicians, and industry representatives.<sup>18</sup>

Potential funding sources for SAFARI include annual participant fees, government funding or awards (FDA, AHRQ, National Institutes of Health [NIH]), or industry funding. Another possibility is to link participation in SAFARI to reimbursement; however, this would require CMS to make an independent decision to implement a national Coverage with Evidence Development (CED) policy. This approach was endorsed by some participants in the meeting as the best way to ensure broad participation in SAFARI and comprehensive data collection. Participants who did not support this approach made the argument that a CED decision is not appropriate for AF ablation because sufficient data are currently available to demonstrate the clinical utility of catheter ablation for the treatment of AF. If a national CED policy is not issued, a mixed model of funding, like the model used to fund the ICD longitudinal study, might be the most plausible.

Safety of Atrial Fibrillation Ablation Registry Initiative could potentially benefit various stakeholders. It could serve as a platform for CED evaluation, if the latter is deemed appropriate by CMS. It could contribute to quality improvement and could enhance guideline adherence. It could inform the development of practice guidelines and competency statements. It could better inform regulatory processes to ensure safety of medical

products used in diagnosis, ablation, and subsequent therapy of AF.

For industry, SAFARI could potentially be helpful in both the pre- and postmarket arenas. Safety of Atrial Fibrillation Ablation Registry Initiative has the potential to provide a mainstream database that may be helpful in hypothesis generation. It may make the regulatory review process more efficient in terms of providing data to develop performance goals and precise point estimates of event rates to be used in sample size and power calculations. It may also serve as a construct for conducting postapproval studies. Therefore, SAFARI has the potential to decrease research and development costs and time delays for manufacturers. Whether an effort like SAFARI could have a significant impact on the burden of premarket studies of new devices or device technologies for AF ablation remains to be seen.

Safety of Atrial Fibrillation Ablation Registry Initiative could also impact postmarket studies. By filling knowledge gaps, SAFARI can enhance the FDA's mission to continue to ensure the safety and effectiveness of marketed medical devices as they are adopted into practice. Safety of Atrial Fibrillation Ablation Registry Initiative has the potential to aid in the surveillance of well-defined outcomes of interest. It might be considered a data source for the FDA's Sentinel Initiative, providing useful surveillance and observational study capabilities.<sup>19</sup> Finally, SAFARI could be useful as a platform into which studies could be nested including randomized studies of monitoring strategies or adjunctive therapies. This vehicle could not only fulfill postapproval study requirements for ablation devices efficiently, but leverage expanded indications for drug adjuncts and/or inform best practices for professional society guidelines.

## SAFARI and the future

The leadership of SAFARI, the CSRC, and the ACC came to an agreement to work toward implementation of the SAFARI vision, incubated through CSRC, as an ACC-NCDR registry of AF ablation. Before the end of 2010, this agreement will be implemented. Specifically, identification of a strategic plan for establishing a sustainable funding mechanism and appointment of the members of the leadership of such an NCDR registry will begin. In this plan, ideally, the leadership and governance structure of an NCDR registry will leverage the expertise of the existing SAFARI leadership, within the clearly defined ACC-NCDR policies regarding registry oversight, data access, publication, and overall governance.

Participants in the meeting agreed that SAFARI should be able to adapt to new discoveries such that, when new techniques and therapies emerge, their impact and safety can be systematically tracked. To that end, CRFs will need to be reevaluated and potentially updated when new technologies become available. This task could be

assigned to the CRF working group with input from a statistics and data management committee.

Many have argued that SAFARI should fit in with other AF trials and registry efforts. It should help standardize data elements for single-center registries and future multicenter registries. To ensure valid comparisons, future registries should attempt to use similar data definitions to those used in SAFARI and CABANA. However, it was importantly noted that the specific objectives of SAFARI should avoid undue overlap with other trials and registries because human clinical research should not be unnecessarily duplicative. That coupled with limited resources calls for care in SAFARI's final design. Not only should the purpose and scope of this registry be defined explicitly, but the goals need to be clear and attainable. Every attempt will be made to ensure that SAFARI complements rather than duplicates other initiatives in AF ablation.

One unique area of SAFARI's potential reach is in conjunction with the CSRC's focus on obligatory drug-device safety interactions. It will be important to gather data regarding drugs used before and after AF ablation in SAFARI. Although ablation and antiarrhythmic and antithrombotic drug therapies are intuitively complementary and are commonly used in combination, center-to-center variability in approach to drug use exists; and guidelines on the safest and best practice are still immature. Thus, examining this variability should be one of the unique objectives of SAFARI.

Embedding prospective RCTs into ongoing SAFARI data collections was deemed by many participants in the meeting to be creative and quite attractive; however, the logistics, ethics, and design of such embedded studies, like so many aspects of this unique public health effort, will require careful consideration.

## Conclusions

Over the course of 9 months between the initial and follow-up SAFARI meetings, substantial organizational progress has occurred. In addition, SAFARI is increasingly recognized as an initiative that has the potential to provide important information on AF ablation in routine clinical practice especially in relation to this procedure's safety, effectiveness, and durability. It can help improve quality and can offer a platform for benchmarking, quality measure development, and postmarket product surveillance.

As an ongoing registry, SAFARI may also provide an adaptable and systematic way to follow safety in the rapidly evolving arena of device and drug therapy of AF. Final ratification of the SAFARI charter, continued refinements to the CRF instruments to ensure clarity and minimize site burden, and solutions to key issues such as funding are the current focus to complete phase 0 and move into the pilot phase 1. Continued support

from electrophysiologists who perform AF ablation and their professional organizations (HRS, ACC) will be critical to the success of this registry. If prudently developed and launched, SAFARI has the potential to inform and thereby improve the care of patients undergoing AF ablation.

## Disclosures

**Disclaimer:** The views expressed in this paper reflect the opinions of the authors only and do not necessarily represent regulations and policies of the FDA, AHRQ, Department of Human Services, or the authors' affiliated organizations.

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## **Appendix A.**

### **Meeting participants**

Participants from academia and clinical practice: Sana M Al-Khatib, MD, MHS; Hugh Calkins, MD; Kenneth Ellenbogen, MD; Daniel Frisch, MD; Ann Garlistki, MD; Alan Go, MD; David Haines, MD, FACC; Stephen Hammill, MD; Steven Hao, MD; Warren Jackman, MD; Mohammed Khan, MD; Robert Kowal, MD, PhD; Peter Kowey, MD; Mitchell Krucoff, MD; Dhanunjaya Lakkireddy, MD; Andrea Natale, MD; John Onufer, MD; Douglas Packer, MD; John Rumsfeld, MD; Jeremy Ruskin, MD; Andrea Russo, MD; Philip Sager, MD; Mintu P. Turakhia, MD, MAS; Linda Umbarger, RN, BGS; Niraj Varma, MD, PhD; Paul Varosy, MD; Albert Waldo, MD; David J. Wilber, MD.

Participant from the CMS: Marcel Salive, MD.

Participants from the US FDA: Felipe Aguel, PhD; Randall Brockman, MD; Jun Dong, MD, PhD; Benjamin Eloff, PhD; Libet Garber; Thomas Gross, MD, MPH; William MacFarland, MS; Elias Mallis; Danica Marinac-Dabic, MD, PhD; Ellen Pinnow, MS; Jeremiah Wille.

Participants from the NIH: Alice Mascette, MD; Yves Rosenberg, MD, MPH.

Participants from the AHRQ: Elise Berliner, PhD.

Participants from the ACC: Ralph Brindis, MD, MPH; Janet Wright, MD; Susan Fitzgerald, MD; Kristi Mitchell, MPH; Mary Ann Elma; Janet S. Wright, MD, FACC.

Participants from the HRS: Laura Blum; Kathryn Pontzer.

Participants from the American Hospital Association: Nancy Foster.

Participants from industry: Burke Barrett; Joel Becker, MBA; Julie Broderick, MSc; Mark Carlson, MD; David Curd, MS; Ruey Dempsey; Mary Donlin; Deborah Fleetham; Emily Forbes; Kenji Fujita; Dennis Hong; David Kim; Andrew Koren, MD; Steven McQuillan; Jay Millerhagen, MBA; Kevin Mitchell; Laura Nelson; Linda Nelson, RN; Philip Sager, MD; Dan Schaber, PharmD; Kenneth Stein, MD, FACC; Kristine Teich, MBA, RAC; Sharon Thompson, RA; Eric Vang, PhD, MPH; Lynette Voshage-Stahl; Jagruti Vyas; Melissa Walker, MS, RAC; Sarah White, MPH; Claire Williams; Theresa Wright, MD; Marcia Yaross, PhD; Mingdong Zhang, MD, MPH, PhD.

Participants from the coordinating staff: Eva Hill; Valarie Morrow; Lena Wegner from the DCRI.

## **Appendix B.**

### **SAFARI executive committee**

Hugh Calkins, MD; Benjamin Eloff, PhD; Stephen Hammill, MD; Peter Kowey, MD; Mitchell Krucoff, MD; Danica Marinac-Dabic, MD, PhD; Ellen Pinnow, MS; Marcia S. Yaross, PhD.