

G970280 Chronology

A previous IDE G970003 was approved and active at the time of approval for G970280. The IDE G970003 was for the Pathfinder AF System approved for the study of mapping indications. This study was considered and referred to as Phase I. The sponsor modified the device to incorporate temperature sensing capabilities in order to continue with an ablation study. The modified device, Pathfinder AFTC Microcatheter System, was the subject of G970280. The feasibility phase of this study is referred to as Phase IIa and IIb.

AP – Approved AC – Conditionally Approved DI – Disapproved NR – No Response IA – Inadequate Incoming (additional information necessary)
 AK – Acknowledge Incoming **BOLDED** – Full approval of study phase * - Additional information provided in Appendix

Supp. #	Decision Date	Reason	Action	Comments
CONDITIONAL APPROVAL FOR PHASE IIA (FEASIBILITY)				
	12/19/97	Original IDE	AC	Phase IIa feasibility study consisting of 3 sites, 10 subjects for treatment of symptomatic PAF
S002	2/19/98	Change to protocol	NR	Removed initial TTE, removed lab tests and 24 hour Holter at months 1 and 6
S004	5/21/98	Change to protocol to modify an ablation trajectory and propose expansion to 15 pts	AP/DI	Ablation trajectory change was AP, but expansion was DI due to request for progress report of the first 10 patients
S005	5/29/98	Response to AC letter dated 5/1/98	AP	Full approval of the study (Phase IIa)
S009	9/3/98	Annual report	NR	Teleconference outlining future concerns including one regarding the high number of protocol deviations
S010	9/11/98	Expansion of study to 12 pts	AP	
CONDITIONAL APPROVAL FOR PHASE IIB / DISAPPROVAL FOR PIVOTAL (EXPANDED FEASIBILITY)				
S013*	12/11/98	Request expansion to 15 sites, 80 patients	DI/AC	DI for this request because the data did not demonstrate that device will provide a clinically acceptable acute effectiveness; AC for 5 sites and additional 20 patients called Phase IIb - limited safety and effectiveness - requesting effectiveness hypothesis of a clinically relevant percent reduction of episodes among other issues 32 patients (IIa: 12; IIb: 20)
S016	1/28/99	Request total of 8 sites	AP	
S020	5/13/99	Response to AC letter dated 12/11/98	AC	AC for 8 sites and 30 pts; FDA letter requested updated protocol 42 patients (IIa: 12; IIb: 30)
S021*	5/21/99	Response to AC letter dated 12/11/98	AC	FDA letter requested revision of safety endpoint, info regarding QoL, sample size info, info regarding reporting bias, and regression to the mean
S022	5/27/99	Request additional 15 patients	AC	57 patients (IIa: 12; IIb: 45)
S023*	6/18/99	Request expansion to 9 sites and 70 subjects	AP	70 patients (IIa: 12; IIb: 58)
S025	7/21/99	Response to AC letter dated 5/27/99	AP	
S026	7/21/99	Response to AC letter dated 5/21/99	AC	FDA letter requested revised effectiveness endpoint and sample size calculation outlining future concerns regarding QoL
S027*	8/25/99	Request total of 80 subjects, addition of Revelation	AP	80 patients (IIa: 12; IIb: 68)

Supp. #	Decision Date	Reason	Action	Comments
		Tx, modification of follow-up for self-reporting, and change to anticoagulation		
S034*	3/10/00	Letter informing FDA that an IDE supplement would soon be submitted for request for approval of NavAblator	NR	
S035*	4/7/00	Request to allow investigators to perform second ablation if necessary, allow enrollment of patients refractory to amiodarone only, allow patients who failed initial enrollment (due to AF frequency too low) to reapply for study enrollment after 6 months, and addition of 1 site	AC	FDA letter requested blanking period for second ablation and stating that any patient treated with a non-investigational catheter during the blanking period should be considered an acute failure
S036*	4/21/00	Request for meeting to discuss pivotal protocol	NR	Meeting minutes provided
S037	4/21/00	Response to 7/21/99 letter	AP	Future concerns: (1) changing confidence intervals and sample size to reflect expected success rates, (2) consider stratifying patients into 2 groups of either high or low density AF, and (3) QoL assessment
CONDITIONAL APPROVAL FOR PHASE III (PIVOTAL)				
S038	6/8/00	Request addition of 128 pts (total 208) and add the NavAblator	AC/AP	FDA letter requested clearly stated study hypotheses for Phase III and description of statistical methods used to test the hypotheses for Phase III (15 sites) 208 patients (IIa: 12; IIb: 68; III: 128)
S039*	8/18/00	Response to 6/8/00 AC letter, request additional sites, eliminate use of Holter monitoring	AP	
S042*	5/9/01	Annual report	IA	FDA letter requested (1) Cardima develop a plan to decrease number of protocol deviations specifically compliance with follow-up monitoring and (2) non-consistent definition and measurement of acute success
S045	8/29/01	5 Day Notice for a change in enrollment requirement to 6 episodes in 60 days rather than 3 in 30	NR	
S047*	12/13/01	Change in protocol for adverse events and endpoint definition	AP	
S051	6/10/02	Request additional 72 patients (total 280)	AP	280 patients (IIa: 12; IIb: 68; III: 200)
PMA (P020039) SUBMITTED				
S054*	1/10/03	Request additional 50 patients and request change to allow only use of Revelation Tx and NavAblator	AP	330 patients (IIa: 12; IIb: 68; III: 250)
S057	5/26/04	Annual report	OT	FDA letter indicating a new RCT is needed based on 5/21/04 NOAP letter

Chronology of Cardima Revelation Tx Microcatheter and NavAblator System (P020039)

MAJR – Major Deficiency NOAP – Not Approvable * Additional information provided in Appendix

Supp. #	Received Date	Reason	Action	Decision Date	Comments
ORIGINAL PMA SUBMISSION					
Orig.*	9/23/02	Clinical Module (Original PMA)	MAJR	11/14/02	MAJR letter requested additional (1) data for NavAblator, (2) pt info, (3) episode reduction info, (4) AE info, (5) justification for pooling pt data, (6) info regarding QoL secondary endpoints, (7) info regarding acute procedural endpoint, (8) assessment of compliance w/ mandatory TTM recordings, (9) details of baseline monitoring period, (10) inclusion of withdrawn pts, (11) info regarding 6 mo follow-up for all pts, (12) adequacy of sample size, (13) info regarding paired t-tests, and (14) statistical info by clinical site and pt demographics.
A002*	1/16/03	Response to 11/14/02 MAJR letter (amendment received 1/16/03)	NOAP	6/26/03	NOAP letter concurred with 5/29/2003 panel's 7-0 vote for disapproval. Letter outlined the following issues: (1) lack of an accurate measurement of effectiveness endpoints, (2) bench testing demonstrating lesion comparison, (3) customer experience reports, and (4) shelf life not adequately demonstrated.
		Circulatory Systems Advisory Panel Meeting		5/29/03	Panel voted 7-0 against approval
AMENDMENT 6 OF PMA SUBMISSION					
A006*	1/21/04	Response to 6/26/03 NOAP letter	NOAP	5/21/04	A006 focuses only on Phase III pts adding 34 pts for a total of 84 included in primary effectiveness endpoint and also addresses questions 2-4 of 6/26/03 letter. NOAP letter states that issues in 6/26/03 letter still remain and outlines future study concerns (need for RCT) and some outstanding sterility concerns.