Summary of Safety and Clinical Performance (SSCP) for vCLAS Cryoablation Catheter

(PM-006 Rev. E)

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1 MEDICAL DEVICE IDENTIFICATION & GENERAL INFORMATION

Device trade name	vCLAS™ Cryoablation Catheter
Generic Name	VT Cryoablation Catheter
Model Number	P/N 109-0017-001
Manufacturer's name and address	Adagio Medical, Inc. 26051 Merit Circle, Suite 102, Laguna Hills, CA 92653
Manufacturer's single registration number (SRN)	US-MF-000001129
Basic Unique Device Identification Device Identifier (UDI-DI)	0850037705109-0017-001D2
Medical device nomenclature description / text	C020302 Arrhythmogenic foci cryoenergy ablation leads
Class of device	class III
Year when the first certificate (CE) was issued covering the device	TBD (pending CE-mark application with TUV SUD)
Authorized representative	QualRep Services B.V. Utrechtseweg 310 – Bldg B42, NL-6812 AR Arnhem, The Netherlands
Authorized representative's SRN	NL-AR-000000537
Notified Body Name and Identification Number	TÜV SÜD Product Service GmbH, 0123

2 INTENDED USE OF THE DEVICE

2.1 Intended Purpose

The vCLAS™ Cryoablation Catheter, a component of the Adagio Medical Inc. VT Cryoablation System is intended to create transmural linear and focal lesions to cardiac structures within the endocardium of the ventricles with cryoablation.

2.2 Indication(s) and target population(s)

- **Indication:** The Adagio Medical Inc. VT Cryoablation System (Catheter and Console) is indicated for the treatment of monomorphic ventricular tachycardia by ablation of arrhythmogenic tissues that drive and maintain these arrhythmias.
- **Target Population:** The Adagio Medical Inc. VT Cryoablation System (Catheter and Console) is used in patients suffering from monomorphic ventricular tachycardia. Reference section Contraindication for more details.

2.3 Contraindications for Use

Adagio Medical Inc. VT Cryoablation System (Catheter and Console) is contraindicated as follows:

- In patients with a systemic infection
- In patients with intracardiac thrombus
- In patients with cryoglobulinemia
- In pediatric patients (below the age of 18)
- In pregnant or breastfeeding patients
- In patients with hypercoagulopathy or an inability to tolerate anticoagulation therapy during an electrophysiology procedure
- In patients with an interatrial baffle or patch as the transseptal puncture could fail to close
- In patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe.

3 DEVICE DESCRIPTION

3.1 Device Description

The Adagio Medical vCLAS™ Cryoablation Catheter (VT Cryoablation Catheter or Catheter) is a single use device intended for percutaneous delivery and endocardial ablation of ventricular substrate in the treatment of ventricular tachycardia. It is designed to be used together with Adagio Medical VT Cryoablation Console (Cryoablation Console or Console) and related components as a part of Adagio's VT Cryoablation System.

The Catheter connects to the Cryoablation Console via Proximal Connector (**Figure 1**) and Console's Connection Port, creating a closed loop that circulates cryogenic near-critical nitrogen (CN2) from the Console to the 15 mm long Cryoablation Element of the Catheter. This enables the Cryoablation Element to reach cryogenic temperatures and to create therapeutic, transmural linear and focal lesions. The Cryoablation Element temperature is continuously monitored by two internal thermocouples and displayed on the Cryoablation Console.

The Catheter is compatible with approved 10F (or greater) steerable and fixed-curve guide sheaths (see device IFU for details). Vascular access is obtained by standard femoral vein and/or femoral artery puncture.

The Cryoablation (Freezing) Element of the Catheter contains eight (8) 1mm electrodes distributed evenly with 1mm spacing (Figure 1). The electrodes provide EGM recording and pacing capability when no ice formation is present. The EGM monitoring and pacing are accomplished via standalone Electrophysiology (EP) Recording System. The EP Recording System is a standalone medical device used for recording and monitoring of electrocardiograms (ECG) to map and diagnose ventricular tachycardia. The Catheter connects to the EP recording system via Distal Electrode Connector and standard adapter cable. The EP Recording systems use universal junction box and adapter cables. The Catheter is compatible with any junction box of commercially available EP Recording Systems.

The distal portion of the Catheter (Figure 1), Articulation Segment) supports bi-directional deflection of Cryoablation Element by 180º, as controlled by the actuator and turning knob within Catheter's Handle

Assembly. The turning knob adjusts the resistance of the deflection up to positional lock at any desired deflection angle.

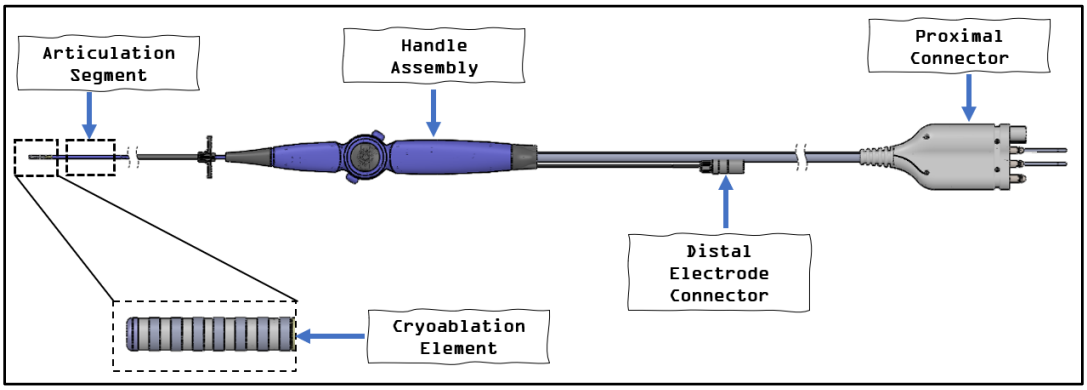

Figure 1: vCLAS Cryoablation Catheter

The following table identifies design characteristics for the Catheter.

Table 1 VT Cryoablation Catheter Design and Performance Characteristics

Design Characteristic			
Key Functional Element with Patient Contact	**Characteristics**	**Dimensions**	**Patient Contact Materials**
	Image of the Cryoablation Element of VT Cryoablation Catheter		See below
Outer shaft	Shaft Diameter	9 Fr	Pebax, Barium sulfate and pigments
	Total Length (Usable)	115 cm	
Cryoablation element	Freezing Element & Tip Length	15 mm	
Articulation element	Articulation Segment Length	65 mm	Pebax, Barium sulfate and pigments
	Deflection	180 degrees (bi-directional)	
Electrodes	Electrodes	8	Pt/Ir
	Electrode Size	1 mm	
	Electrode Spacing	1 mm	

Cryoablation tip	Freezing Tip	Yes	Stainless steel containing Cobalt
Performance and Other characteristic			
Cryoablation Performance	≤ -100°C achieved within 30 seconds		
Environmental Parameters	Non-pyrogenic Single Use Sterilization: EO		

3.2 Principles of operation of the device and its mode of action

The System is used to create transmural linear and focal lesions to endocardial tissues in the ventricles, providing greater assurance that the arrhythmogenic substrates are eliminated or isolated, thus restoring a normal cardiac rhythm. The Console contains an internal reservoir of liquid nitrogen that is used to pre-cool the CN2 cryogen to approximately -196°C. This cryogen is then delivered to the Catheter where it circulates within closed, internal lumens that are surrounded and insulated by a vacuum channel. The targeted cardiac tissue is exposed to cryogenic temperatures at the only non-insulated portion of the Catheter. This non-insulated portion is located at the distal tip and referred to as the Cryoablation Element (freezing & treatment zone), which is continuously monitored and measured by an internal thermocouple. The Catheter is delivered to the ventricles of the human heart via venous/arterial access following trans-septal and retrograde approach. Using a compatible guide sheath approved by Adagio, the Catheter is positioned such that the Cryoablation Element is adjacent to the targeted tissue. The articulation segment of the Catheter facilitates accurate position of the catheter (cryoablation element) geometry over the anatomies of importance. After the desired position and catheter-tissue contact have been obtained, a freeze cycle is initiated through the interactive touch screen on the Console. The chilled CN2 fluid will begin circulating through the catheter and delivering treatment to the tissue adjacent to the cryoablation element. The tissue that is in contact with the Cryoablation Element (freezing element) will cool to cryogenic temperatures, resulting in necrosis (ablation) of the tissues and the creation of linear and/or focal lesions. After the cryogen circulates back into the Console, it is automatically heated up to ambient temperature and safely vented into the atmosphere.

3.3 A reference to previous generation and description of the differences

Not applicable. There is no previous generation or any device similar to the VT Catheter.

3.4 Description of any accessories which are intended to be used in combination with the device

The Catheter is designed to be used in combination with the following non-active devices and accessories that are sold separately:

Steerable ≥10 Fr guide sheaths: the Catheter is designed to be compatible with steerable ≥10 Fr guide sheath for vascular access and navigation to target tissues. The use of a guide sheath unapproved by Adagio may damage the catheter and the sheath.

Adagio approved guide sheaths:

- Oscor Destino™ Reach (10 F)
- Abbott Fast-Cath Mullins (10 F)

3.5 Description of any other devices and products which are intended to be used in combination with the device

The Catheter is designed to be used in combination with the following active devices that are sold separately:

- Cryoablation Console : The Catheter is connected to the Console via a connector to allow cryogen delivery and monitoring of the ablation critical parameters (temperature, pressure, and flow etc.) during operation.
- Commercial Electrophysiology (EP) System: The Catheter is connected to the EP system via the electrical connectors.

4 RISKS AND WARNINGS

4.1 Residual risks and undesirable effects

Based on safety data from the CryoCure-VT study, the VT Cryoablation System offers a similar safety profile as compared to the current RF technology. The following residual risks and undesirable effects are disclosed in the device IFU based on the report rates in literatures[1,2,3] and data from the CryoCure-

[1] Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, Aguinaga L, Leite LR, Al-Khatib SM, Anter E, Berruezo A, Callans DJ, Chung MK, Cuculich P, d'Avila A, Deal BJ, Della Bella P, Deneke T, Dickfeld TM, Hadid C, Haqqani HM, Kay GN, Latchamsetty R, Marchlinski F, Miller JM, Nogami A, Patel AR, Pathak RK, Sáenz Morales LC, Santangeli P, Sapp JL, Sarkozy A, Soejima K, Stevenson WG, Tedrow UB, Tzou WS, Varma N, Zeppenfeld K; ESC Scientific Document Group. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. Europace. 2019 Aug 1;21(8):1143-1144. doi: 10.1093/europace/euz132. Erratum in: Europace. 2019 Aug 1;21(8):1144. Erratum in: J Arrhythm. 2020 Jan 12;36(1):214. Erratum in: Europace. 2020 Mar 1;22(3):505. PMID: 31075787; PMCID: PMC7967791

[2] Ding WY, Pearman CM, Bonnett L, Adlan A, Chin SH, Denham N, Modi S, Todd D, Hall MCS, Mahida S. Complication rates following ventricular tachycardia ablation in ischaemic and non-ischaemic cardiomyopathies: a systematic review. J Interv Card Electrophysiol. 2022 Jan;63(1):59-67. doi: 10.1007/s10840-021-00948-6. Epub 2021 Jan 29. PMID: 33512605; PMCID: PMC8755671

[3] Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, Gonzalez MD, Worley SJ, Daoud EG, Hwang C, Schuger C, Bump TE, Jazayeri M, Tomassoni GF, Kopelman HA, Soejima K, Nakagawa H; Multicenter Thermocool VT Ablation Trial Investigators. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the multicenter thermocool ventricular tachycardia ablation trial. Circulation. 2008 Dec 16;118(25):2773-82. doi: 10.1161/CIRCULATIONAHA.108.788604. Epub 2008 Dec 8. PMID: 19064682.

VT study.

Frequent (>5%)	
• Arrhythmia recurrence • Death • Arteriovenous (AV) fistula • Femoral artery occlusion • Femoral vein occlusion	• Groin hematoma/ecchymosis/vascular complications • Obstruction or perforation or damage to vascular system • Retroperitoneal bleed
Probable (1 – 5%)	
• Acute periprocedural hemodynamic/cardiogenic shock • Air/gas embolism • Chest pain/discomfort • Heart block • Bundle branch block • Cardiac arrest • Cardiac perforation/tamponade • Cardiac thromboembolism • Cerebral infarct (hemorrhagic or thromboembolic) • Congestive heart failure/ pulmonary edema • Coronary artery damage • Left ventricular pseudoaneurysm	• Major bleeding, requiring surgery or transfusion • Myocardial infarction • Pericardial effusion • Pericarditis • Pleural effusion • Infection/sepsis • Prolonged procedure • Prolonged recovery • ST segment elevation • Thromboembolism • Transient ischemic attack (TIA) • Valve damage such as Aortic and/or Mitral, Tricuspid
Occasional (<1%)	
• Acute respiratory distress syndrome (ARDS) • Allergic reaction/anaphylaxis • Anemia • Anesthesia reaction • Aorto-right atrial fistula • Dislodgement of pacemaker • Electric shock • Elevated cardiac enzymes • Endocarditis • Femoral nerve injury/palsy • Fever	• Fluid overload • Hypotension/Hypertension • Hypothermia • Pneumonia • Pulmonary bronchi thermal injury • Radiation injury • Respiratory depression • Skin burns • Tissue damage related to cryo injury • Vasovagal reactions

4.2 Warnings and precautions

- **Anticoagulation -** Administer appropriate peri-procedural anticoagulation therapy per standard of care for patients undergoing cardiac ablation therapy in left and right ventricles. Administer anticoagulation therapy during and post-procedure according to local institution standards to minimize bleeding and thrombotic complications.
- **Approved Guide Sheaths** – Use only approved guide sheaths. Refer to the IFU for the brands and models of the approved sheaths to be used with the Catheter.

  - The use of an unapproved guide sheath may cause damage to the Catheter and to the sheath and may lead to serious patient injury.
  - Follow the guide sheath manufacturer's IFU to deploy the sheath. For the Mullins sheath, always use the supplied dilator in the sheath lumen before venous/arterial access to avoid sheath damage.
- **Biohazard Disposal** - Dispose of the Catheter in accordance with hospital procedures and local regulatory and biohazard standards.
- **Catheter Manipulation** - Extreme care must be utilized during catheter manipulation to avoid Catheter damage, cardiac damage and/or perforation. The Catheter should be deployed in the middle of the cardiac chamber.

Do not use excessive force to advance, withdraw, deflect, or rotate the Catheter, especially if resistance is encountered. Excessive force may lead to catheter damage, including kink or cryogen leakage.

- **Carcinogenic, Mutagenic, Reprotoxic (CMR) Substance –** The device is known to contain Cobalt (CAS #7440-48-4), a CMR substance. All materials with direct patient contact were tested and met Biocompatibility requirements.
- **Cryo-adhesion** - During cryoablation, the cryoablation element adheres to the cardiac tissue and may adhere to the guide sheath. Do not attempt to manipulate the Catheter during or after cryoablation cycle until sufficient evidence of lack of adhesion to tissue or guide sheath is observed by ensuring the Catheter Distal Temperature (T_D) reaches a minimum of 30ºC, the minimum of 60 second Thaw cycle is complete, and interference seen on the EGMs during the freeze disappears. Do not rotate, pull, remove, or otherwise manipulate a Catheter that resists movement.
- **Device Integrity -** Do not use the Catheter if visual inspection shows bumps, kinks, or other damage. If there is a suspicion the Catheter may be damaged or kinked while in patient, it should be carefully removed, visually inspected, and performed FULL FUNCTIONAL TEST (Console Operator's Manual **Section 10.3.12**) outside of the patient. If any damage is confirmed, the Catheter shall not be reinserted in the patient and must be returned to Adagio Medical, Inc.
- **Device Sterility** – The Catheter is supplied sterile. Inspect sterile packaging (all seals) for any signs of damage such as holes or compromised seal integrity prior to opening and removal of the device. If damaged, do not use it and return to Adagio Medical, Inc.
  - The Catheter is for single use only. Do not reuse, reprocess, or re-sterilize, as this will compromise device integrity and function and may lead to patient illness, injury, or death.
- **Embolism Risk** - Introducing catheters and sheaths into the circulatory system may result in air emboli. Use proper endovascular techniques to minimize the risk of embolization, including flushing the sheath prior to catheter insertion.
- **Interaction With Implantable Cardiac Defibrillators (ICDs) and ICD Leads** – VT patients are often implanted with ICDs as protection from Sudden Cardiac Death. Disable ICD operation prior

to performing cryoablation and use temporary devices to support pacing and defibrillation during the procedure. Do not perform cryoablation when the Catheter's Cryoablation Element is in direct contact with ICD lead(s).

- **Interaction With Other Devices** - Use caution when there are diagnostic catheter(s) in the cardiac chamber in addition to the Catheter. No freeze should be initiated unless it is confirmed that other catheters are not in contact with the Catheter's cryoablation element. To avoid entangling the catheters, it is recommended to manipulate different catheters sequentially, keeping them as far apart as possible.
- **Package Integrity** – The Catheter is supplied individually packaged within a pouch and a box. Package contents are listed on the pouch and box labels. Do not use it if labeling is illegible or incomplete. Check expiration date shown on the label. Do not use the Catheter beyond the expiration date.
- **Pressurized Cryogen** – The Catheter contains pressurized NCN cryogen during operation.
  - The Catheter reaches cryogenic temperatures. Do not touch the cryoablation element when cryogenic energy is delivered by the Cryoablation Console as operator injury may occur.
  - The application of cryogenic temperature results in permanent damage to cardiac tissues. Ensure the cryoablation element is in contact only with the target tissue prior to initiating energy delivery.
  - If the Catheter develops an external leak, patient injury (such as air/gas embolism) or death may occur. **CONTINUOUSLY** monitor the catheter proximal temperature on the Cryoablation Console display during cryogen delivery. If the catheter's proximal temperature (T_P) decreases below - 10°C (indicating potential cryogen leak), **IMMEDIATELY DISCONNECT** and **REMOVE** the Catheter.
- **Real-time Cardiac Imaging** - All Catheter maneuvers within the patient (advancement, retraction, deflection, manipulations) must be performed under fluoroscopic guidance or using other real-time imaging modalities capable to accurately identify anatomic and relative position of the devices. Compatible imaging modalities are specified in the IFU**.**
- **Repeat Insertion of the Catheter** – Repeat insertions of the catheter into the guide sheath increases the risk of catheter damage. Visually inspect the catheter and perform a FULL FUNCTIONAL TEST before every reinsertion.
- **Transitory Cardiac Ischemic Events** – Cryoablation carries a small risk of transitory cardiac ischemic events. Monitor for signs of transitory cardiac ischemia using 12-lead ECG and/or internal cardiac electrograms. Stop energy delivery if clinically meaningful signs of ischemia are detected and allow the cryoablation element to fully thaw. Reassess ablation location using imaging modalities and Catheter electrograms displayed on EP System and relocate the Catheter as necessary.
- **X-ray Exposure** - The use of fluoroscopy during electrophysiology procedures may present the potential for significant X-ray exposure. Attention should be given to potential radiation exposure associated with the cryoablation procedure, taking steps to minimize exposure.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

Not applicable. There has been no FSCA or FSN for the Catheter.

5 SUMMARY OF CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP (PMCF)

5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable. There is no equivalent device of the Catheter.

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

The safety and performance of the vCLAS Catheter for the treatment of monomorphic VT are successfully demonstrated and supported by the data obtained from the CryoCure-VT clinical investigation (NCT04893317).

5.2.1 Study Design

CryoCure-VT was a prospective, single-arm, open-label, and multicenter study to evaluate safety and performance of the VT Cryoablation System including vCLAS Catheter. Up to sixty (60) patients with Monomorphic VT have been enrolled in eight (8) clinical centers located in Belgium, France, The Netherlands, Germany, Czech Republic, and Canada. All patients' follow-up has been planned for 1-year with visits at 30-day, 3-, 6- and 12-months post procedure.

5.2.2 Study Methods

The ablation strategy consisted of targeting VT locations identified during the procedure VT recurrence is confirmed with ICD event recording check during follow-up visits at 3, 6, and 12 months along with any safety events. No formal hypothesis testing was prespecified and no control group was available for comparison. Descriptive statistics for all variables were applied.

The objective of the study is to demonstrate the safety and performance of the VT Cryoablation System in patients with monomorphic VT.

5.2.3 Study Population

The study population for the CryoCure-VT

clinical study includes male and female patients, ages 18-80, and scheduled for an endocardial ablation of monomorphic VT (new onset VT and/or VT despite antiarrhythmic therapy). Subjects are included without discrimination by gender, race and/or ethnicity.

5.2.3.1 Inclusion Criteria

Subjects meeting all the inclusion criteria were eligible for the study. These included:

IC 1 Male or female the ages of ≥ 18 years

IC 2 Eligible for a catheter ablation due to Ischemic and/or non-ischemic recurrent symptomatic sustained monomorphic Ventricular Tachycardia also defined as having a similar QRS configuration from beat to beat.

IC 3 Has or will be receiving an ICD prior to hospital discharge post procedure.

IC 4 Refractory to at least one AAD (Refractory is defined as an AAD not able to treat the arrhythmia satisfactorily or induces unwanted side effects).

IC 5 Subject has LVEF > 20%, confirmed by echo or comparable technique in the previous 3 months or during baseline evaluation

IC 6 Willingness, ability, and commitment to participate in baseline and follow-up evaluations for the full length of the study

IC 7 Willingness and ability to give an informed consent

5.2.3.2 Exclusion Criteria

Subjects meeting all the inclusion criteria were eligible for the study provided none of the exclusion criteria were met. Exclusion criteria included:

EC 1 Any known objective contraindication to a ventricular tachycardia ablation, TEE, or anticoagulation, including but not limited to the identification of any cardiac thrombus or evidence of sepsis

EC 2 Any duration of continuous arrythmia that is not monomorphic ventricular tachycardia. Multiple monomorphic tachycardia is acceptable, but polymorphic VT is not.

EC 3 Any VT ablation within 4 weeks prior to enrollment

EC 4 More than one prior (> 4 weeks) VT ablation or prior surgical treatment for ventricular tachycardia

EC 5 Ventricular tachycardia secondary to electrolyte imbalance, active thyroid disease, or any other reversible or non-cardiac cause

EC 6 Structural heart disease as described below:

a. Class IV heart failure
b. Aortic aneurysm
c. Previous cardiac surgery or percutaneous intervention within 60 days prior to index procedure
d. Interatrial baffle, closure device, patch, or PFO occlusion device
e. IVC filter
f. Coronary artery bypass graft (CABG) procedure within six (6) months prior to procedure
g. Severe Mitral or Aortic insufficiency or stenosis based on most recent TTE
h. Cardiac myxoma
i. Significant congenital anomaly
j. Recent Myocardial Infarct (MI) or unstable angina, within 60 days prior to the ablation procedure
k. Mechanical mitral or aortic valve

EC 7 Any previous history of cryoglobulinemia

EC 8 History of blood clotting or bleeding disease

EC 9 Any prior history of documented cerebral vascular accident (CVA), TIA or systemic embolism (excluding a post-operative DVT), within 6 months prior to the ablation procedure

EC 10 Breastfeeding, pregnant, or anticipated pregnancy during study follow-up

EC 11 Current enrollment in any other study protocol where testing or results from that study may interfere with the procedure or outcome measurements for this study

EC 12 Any other condition that, in the judgment of the investigator, makes the patient a poor candidate for this procedure, the study or compliance with the protocol (includes vulnerable patient population, mental illness, addictive disease, candidate for heart transplantation, patient with ventricular assist device, or terminal illness with a life expectancy less than 12 months).

5.2.4 Endpoints and Results

The safety and performance of the System for the treatment of ventricular tachycardia are successfully demonstrated and supported by the data obtained from the ongoing CryoCure-VT clinical investigation interim results. The CryoCure-VT is an ongoing clinical study where cryogenic energy was applied to create a scar to destroy the tissue that causes VT. As of data cut-off date of 19July, 2023, Sixty-four (64) subjects were enrolled and treated in the study.

Table 2: CryoCure-VT Patients' Baseline Characteristic

Characteristics	Result
Patient Demographics (n=64)	
Mean Age	67 ± 11 years
Male Gender	61 (95%)
Mean Weight	92.7 ± 13.5 kg (59 – 122)
Mean Left Ventricular Ejection Fraction (LVEF)	35.2% ± 9.6%
Medical History (n=64)	
Hypertension	53 (82%)
Diabetes	19 (30%)
Coronary Artery Disease (CAD)	48 (75%)
Congestive Heart Failure	37 (58%)
Significant Valvular Disease	12 (19%)
Cardiomyopathy	57 (89%)
Hypertrophic	4 (6%)
History of Ventricular Fibrillation	9 (14%)

Table 3: CryoCure-VT Patients' Inducibility Pre-Procedure (n=60*)

Total number of induced VTs pre-procedure	132
Number of VTs induced per subject	2.0 ± 1.3

Table 3: CryoCure-VT Patients' Inducibility Pre-Procedure (n=60*)

% hemodynamically stable VTs	46.8% (59/126)
% Clinical VTs	46.8% (59/126)
Cycle length of clinical VTs (msec)	371.9 ± 187

* Four (4) patients were not inducible pre-procedure

Table 4: CryoCure-VT Procedural Data

Access	64
Retrograde	12.5% (8/64)
Transseptal	87.5% (56/64)
Procedure time per subject (min)	185 ± 48 (N=64)
Fluoroscopy time per subject (min)	20 ± 13 (N=62)
Mapping time per subject (min)	34 ± 23 (N=62)
Number of lesions per subject	8.9 ± 4.4 (N=64)
Total freeze duration per subject (sec)	32.7 ± 16 (N=64)

Table 5: Safety and Performance Endpoint Results for the CryoCure-VT Clinical Study

Study Endpoints	Endpoint Description	Interim Results
Safety objectives	The Primary Safety objective is an analysis of the proportion of subjects who are free from definite or probable device/procedure related Major Adverse Events (MAEs) that occur during or within 30 days following the cryoablation procedure. The MAEs are defined below: • Death • MI • Cardiac perforation / pericardial tamponade • Cerebral infarct or systemic embolism • Major bleeding requiring transfusion • Mitral, tricuspid or aortic valve damage resulting in moderate or severe regurgitation	**100%** No Major Adverse Event occurred during or within 30 days following the cryoablation procedure.

Table 5: Safety and Performance Endpoint Results for the CryoCure-VT Clinical Study

Study Endpoints	Endpoint Description	Interim Results
	• Access site complications requiring medical or surgical intervention • Pericarditis • Heart block requiring a permanent pacemaker • Other serious adverse device effects (SADEs), including TIAs	
Performance objectives	The Primary Endpoint for Procedure Performance is an analysis of the proportion of subjects with non-inducible clinical monomorphic VT at the conclusion of the initial cryotherapy ablation procedure.	**94%** 50 of 53* patients had no VT inducible post-procedure
	The Primary Endpoint for Clinical Performance is an analysis of the proportion of subjects receiving a single cryoablation procedure with freedom from ventricular tachycardia lasting longer than 30 seconds or appropriate ICD intervention until the end of the 6 month follow up period.	**63%** 32 out of 51** patients had freedom from VT longer than 30s or appropriate ICD intervention through the 6-month follow up based on the event history stored in the ICD

*Of the 64 subjects, VT inducibility was not attempted in 11 patients' post-procedure. Out of a total of 53 subjects with VT inducibility data available at the end of the procedure, clinical VTs remained inducible in 3 subjects.

** Of 51 subjects reached 6-month follow up as of the cut-off date for this report, one subject withdrew consent before 3-M visit and was excluded from the performance analysis. Of the remaining 51, 19 subjects have had a VT recurrence between discharge and their 6-month follow-up visit.

5.2.4.1 Other Safety Events

There has been a total of twenty-one (21) serious adverse events (SAE) of which:

- Four (4) SAEs (6%, 4 out of 52) have been adjudicated by the DSMB to be probably related to procedure and/or device and are listed below.
    - Pericardial effusion was reported on two (2) patients during the cryoablation procedure. They were adjudicated by the DSMB to be serious adverse events that are "probably related" to the procedure and "not related" to the device.

  - False aneurysm on focal myocardial rupture was reported on (1) one patient during the cryoablation procedure. This was adjudicated by the DSMB to be a serious adverse event that is “probably related” to the procedure and “probably related” to the device.
  - Hemodynamic instability was reported on (1) one patient at the beginning of the procedure prior to introduction of the VT Catheter. This was adjudicated by the DSMB to be a serious adverse event that is “definitely related” to the procedure and “not related” to the device.
  - The four (4) SAEs do not meet definitions of Major Adverse Events as per the study protocol as per the DSMB adjudication; therefore, they do not meet the primary or secondary safety endpoints.
- The remaining seventeen (17) events were adjudicated to be serious and not related to device or procedure.

5.3 Summary of clinical data from other sources, if applicable

Not applicable. No clinical data from other sources.

5.4 An overall summary of the clinical performance and safety

The incidence rate of 0% MAE rate and 6.3% SAEs rate reported in this study is consistent with the HRS Guidance of 2019[1], the RF ThermoCool pre-market study[3] and a meta-analysis[2] showing major complication rates ranging from 9%–18% after VT ablation. The individual safety event rates of the four (4) SAEs related to procedure/ device in the CryoCure-VT study are also within the reference range established based on SOTA[2,3]. The adverse events reported in the CryoCure-VT study are within the rates suggested by the expert consensus statement and benchmark peer-reviewed literature on catheter ablation of ventricular arrhythmias. It is concluded that the residual risks of the Catheter have been reduced to an acceptable level and that the Catheter offers a similar safety profile to the state-of-the-art ablation technology.

Clinical performance results of the CryoCure-VT study reported a 63% freedom from VT or appropriate ICD interventions at 6 months. Published results of the RF ablation reported freedom from VT at 47.3%[3] at 6 months and 53.1% in a recent meta-analysis[4]. This result from CryoCure-VT patients who completed the 6-month follow-up visit is consistent with the range of 47.3 – 53.1% reported in published studies[3,4].

The VT System including the vCLAS Catheter has demonstrated a favorable benefit-risk profile as all the risks have been reduced to an acceptable level. It is concluded that the medical benefits offered by the System outweigh the overall residual risks.

5.5 Ongoing or planned post-market clinical follow-up

PMCF activities will be initiated to proactively collect and evaluate clinical data from the use of device upon CE marked approval.

The PMCF study design consists of a prospective, single-arm, multi-center study of up to 60 patients to collect safety and performance data regarding the use of the device according to its labelling across 15

[4] Lima da Silva G, Nunes-Ferreira A, Cortez-Dias N, de Sousa J, J Pinto F, Caldeira D. Radiofrequency catheter ablation of ventricular tachycardia in ischemic heart disease in light of current practice: a systematic review and meta-analysis of randomized controlled trials. J Interv Card Electrophysiol. 2020 Dec;59(3):603-616. doi: 10.1007/s10840-020-00870-3. Epub 2020 Sep 19. PMID: 32948937

clinical sites in Europe over a period of 6 months.

6 POSSIBLE DIAGNOSTIC OR THERAPEUTIC ALTERNATIVES

The three (3) available treatments for VT include implantable cardiac defibrillator (ICD), antiarrhythmic medications, and catheter ablation:

- Implantable cardioverter defibrillator (ICD): ICD is recommended for patients at risk of life-threatening tachycardia episodes.
- Antiarrhythmic Drugs (AAD): AADs including amiodarone, beta-blockers, calcium channel blockers, may prevent a fast heart rate when taken regularly. (AADs) can be effective in preventing recurrent VT and reducing appropriate ICD shocks.
- Catheter ablation: Catheter ablation (radiofrequency) has been proven to be a safe and effective therapeutic method for VT treatment.

7 SUGGESTED PROFILE AND TRAINING FOR USERS

Ablation procedures using the vCLAS™ Cryoablation Catheter should only be performed in the fully equipped electrophysiology laboratories, by trained healthcare professionals specialized in cardiac electrophysiology and trained in catheter manipulations and cardiac access vis transeptal and/or retrograde access.

The Catheter shall only be used by healthcare professionals who have been trained by Adagio Medical personnel regarding the proper use and advised of any safety recommendations of this Catheter.

8 APPLICABLE COMMON SPECIFICATION(S), HARMONIZED STANDARD(S) OR APPLICABLE GUIDANCE DOCUMENT(S)

Standard	Title	Applicability (Full or Partial)
MDR 2017/745	Medical Device Regulations	Full
MEDDEV 2.7/1. Rev 4	Guidelines on Medical Devices, Clinical Evaluation: A Guide for Manufacturers and Notified Bodies	Full
MDCG 2020-13	Clinical evaluation assessment report template	Full
MDCG 2020-7	Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies	Full
IMDRF MDCE WG/N65 FINAL:2021	Post-Market Clinical Follow-Up Studies	Full
ISO/TR 20416:2020	Medical devices — Post-market surveillance for manufacturers	Full
EN ISO 20417: 2021	Medical devices — Information to be supplied by the manufacturer	Full
EN ISO 13485:2016/A11: 2021	Medical devices -- Quality management systems -- Requirements for regulatory purposes	Full

Standard	Title	Applicability (Full or Partial)
EN ISO 10555-1: 2013/A1:2017	Sterile, single-use intravascular catheters - Part 1: General requirements	Full
EN ISO 10993-1:2020	Biological evaluation of medical devices – Part 1: Evaluation and testing	Full
EN ISO 10993-4:2017	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood	Full
EN ISO 10993-5: 2009	Biological evaluation of medical devices – Part 5: Tests for In Vitro Cytotoxicity	Full
EN ISO 10993-10: 2023	Biological evaluation of medical devices – Part 10: Tests for Skin Sensitization	Full
EN ISO 10993-11:2018	Biological evaluation of medical devices – Part 11: Tests for Systemic Toxicity	Full
EN ISO 10993-17	Biological evaluation of medical devices – Part 17: Toxicological risk assessment of medical device constituents	Full
EN ISO 10993-18	Biological evaluation of medical devices – Part 18: Chemical characterization of medical device materials within a risk management process	Full
EN ISO 10993-23:2021	Biological evaluation of medical devices – Part 10: Tests for Irritation	Full
ISO 14644-1:2015	Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration	Full
ISO 14644-2:2015	Cleanrooms and associated controlled environments – Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration	Full
EN ISO 14971:2019/A1:2021	Medical devices – Application of risk management to medical devices	Full
ISO 14698-1:2003	Clean room and associated controlled environment – Biocontamination Control – General principals and methods	Full
IEC 62366-1:2015 A1:2020	Application of usability engineering to medical devices	Full
EN ISO 15223-1:2021	Medical Devices – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirement	Full
ISO 7000:2019	Graphical symbols for use on equipment – Registered Symbols	Full

Standard	Title	Applicability (Full or Partial)
EN 556-1: 2001/AC:2006	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" – Part 1: Requirements for terminally sterilized medical devices	Full
EN ISO 14155:2020	Clinical investigation of medical devices for human subjects-Good clinical practice	Full
EN ISO 11607-1:2020	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems	Full
EN ISO 11607-2:2020 A11:2022	Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes	Full
ISTA 3A	Performance Test for Individual Packaged Product	Full
ASTM F2096-11: 2019	Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)	Full
ASTM D4169-22: 2022	Standard Practice for Performance Testing of Shipping Containers and Systems	Full
ASTM F88/F88M-21: 2021	Standard Test Method for Seal Strength of Flexible Barrier Materials	Full
ASTM F1886/F1886M-16:2016	Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection	Full
ASTM F1980-21:2021	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Device	Full
EN ISO 11135:2014/A1:2019	Sterilization of health care products -- Ethylene oxide -- Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices	Full
ISO 11138-2:2017	Sterilization of health care products -- Biological indicators -- Part 2: Biological indicators for ethylene oxide sterilization processes	Full
EN ISO 11737:2018/A1:2021	Sterilization of medical devices - Microbiological methods - Part 1: Determination of a population of microorganisms on products	Full
EN ISO 10993-7:2008 AMD1:2022	Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals	Full
EN 60601-1: 2006/A1:2013/A2:2020	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance	Full
EN 60601-1-2: 2015/A1:2020	General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests	Full

Standard	Title	Applicability (Full or Partial)
EN 60601-1-6: 2010 (IEC 60601-1-6:2010)	Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard	Full

9 REVISION HISTORY

SSCP Revision	Date issued	Change summary	Revision validated by the Notified Body
A	1May 2023	Initial Release	☒ Yes. Validation language: English ☐ No
B	2 June 2023	Align target population and intended users with the IFU and TF-011	☒ Yes. Validation language: English ☐ No
C	28 July 2023	Update to quantification of residual risks, contraindication, and clinical study results	☒ Yes. Validation language: English ☐ No
D	25 Aug 2023	Aligned Notified body name, updated device description to include design characteristics, added section for materials incorporated into key functional elements and Principles of operation, updated adagio approved guide sheaths, and updated risks in residual risk section.	☒ Yes. Validation language: English ☐ No
E	19 Oct 2023	Aligned intended use, indication for use, target population, contraindication, and intended user. Update clinical performance data. Updated to include warning on device additives.	☒ Yes. Validation language: English ☐ No