Apogee Clinical Investigation Plan (CIP)

Destination Therapy (DT) Post Approval Study (PAS) Addendum

Product Surveillance Registry (PSR) Platform Addendum

Version 2 01DEC2020

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Medtronic

Apogee

Destination Therapy (DT) Post Approval Study (PAS) Addendum
Product Surveillance Registry (PSR) Platform Addendum

Therapy
Heart Failure – Ventricular Assist Devices

Version 2
01DEC2020

Sponsor
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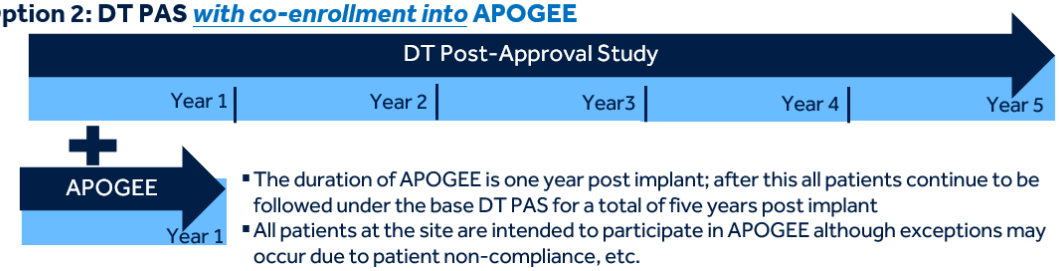
A. Glossary

Term	Definition
ACE	Angiotensin Converting Enzyme
AE	Adverse Events
AKI	Acute Kidney Injury
ARB	Angiotensin II Receptor Blocker
ASA	Aspirin
AVM	Arteriovenous Malformation
BP	Blood pressure
cDV	Color doppler velocimetry
CPB	Cardio-pulmonary bypass
CBC	Complete Blood Count
CRF	Case report form
CT	Computed Tomography
CXR	Chest x-ray
DT	Destination Therapy
ECG	Electro-cardiogram
EGD	Esophago-gastro-duodenal
eGFR	Estimated Globular Filtration Rate
GI	Gastrointestinal
GIB	Gastrointestinal Bleed
HCP	Healthcare provider
ICH	Intracranial Hemorrhage
IFU	Instructions for Use
INR	Internalized Normalized Ratio
IVRT	isovolumetric relaxation time
LDH	lactate dehydrogenase
LV	Left ventricle
LVAD	Left ventricular assist device
MCS	Mechanical Circulatory Support
MR	Mitral regurgitation
mRS	Modified Rankin score
MV	Mitral valve
OR	Operating room
PAS	Post-approval study
PPI	Proton Pump Inhibitor
PRBC	Packed Red Blood Cells
PSR	Product Surveillance Registry
pfHb	Plasma free hemoglobin
POD	Postoperative Day
PT	Pump thrombosis
PT	Prothrombin Time
RHC	Right heart catheterization
RPM	Revolutions per Minute

Term	Definition
TEE	Transesophageal echocardiogram
TTE	Transthoracic echocardiogram
VAD	Ventricular assist device
VCE	Video Capsule Endoscopy

B. Synopsis

Title	**Apogee addendum in Destination Therapy (DT) Post-Approval Study (PAS) patients**
Clinical Study Type	Observational, Non-interventional
Product Name and status	The commercially available HeartWare™ HVAD™ System. Approved patient populations, product purpose, indications and uses of the HVAD System and its components and accessories are defined in the product labeling, instructions for use (IFU), or other applicable manuals.
Sponsor	Medtronic
Indication under investigation	This post-market on-label study is intended to collect data from DT subjects who meet the standard criteria for implantation of a Medtronic HeartWare™ HVAD™ System. No new indications are being explored in this study.
Investigation Purpose	The purpose of the Apogee co-enrollment study is to further enhance scientific understanding of the implant procedure, optimized blood pressure management, and anticoagulation / antiplatelet therapies. The goals of Apogee are: • To evaluate collective impact of Apogee standardized guidelines and characterize impact on 12-month aggregate adverse event rate • To better understand the effects of implant technique and patient management on clinical outcomes
Study Design	DT PAS Sites have the option to co-enroll patients in Apogee. Patients must be consented for the DT PAS to be eligible for participation in Apogee, which will require a separate consent. **Option 1: DT PAS ONLY**  **Option 2: DT PAS *with co-enrollment into* APOGEE** 
Sample Size	The total sample size will be dependent on the number of sites and patients interested in participation in Apogee. If 1/3 of the total DT PAS patients participate in Apogee, the study would be expected to enroll (but not limited to) ~100 patients (1/3 of the total DT PAS patients since the DT PAS enrolls 300 patients).
Inclusion/ Exclusion Criteria	Subjects consented to participate in the DT PAS are eligible for participation in Apogee. There are no exclusion criteria unique to Apogee.

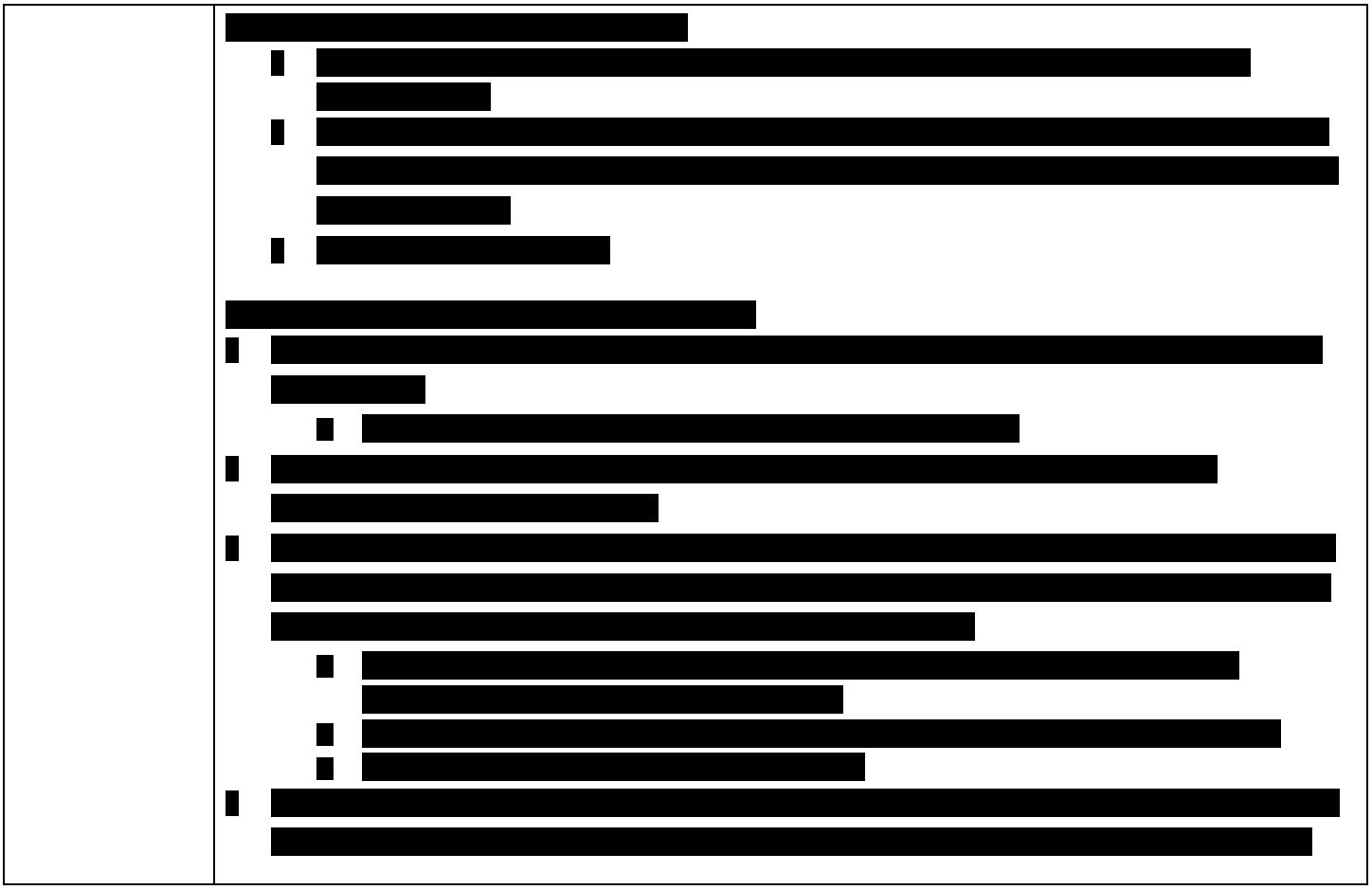
Study Procedures and Assessments	**Apogee Data Collection**

		Enrollment	Baseline	Implant	Discharge	1M F/U	3M F/U	6M F/U	12M F/U	Unsch <12M
	Consent	X								
Implant Procedure	Detailed Implant Collection			X						
	Echo for 2D Velocimetry evaluation		X	X 2 TEEs*	X *With Lavare On x 5 min & Off x 5 min*		X			
	CT Scan Post-implant (send digital image)			X *if performed*						
	Right Heart Cath (RHC) Hemodynamics		X *If subsequent RHC performed*	X *If performed*						
	Chest x-ray (send digital image)			X Post-op						
	Videotape procedure			X *if obtained*						
Blood Pressure	Patient BP Diary**				*Every morning ≥ 40 minutes after taking BP meds and while sitting. Collect whether HCP contacted for values out of range*					
	Medications BP Control				*Consider Medication Guidelines; Report Medication Changes*					
Anticoagulation/Antiplatelet	Home INR monitoring				*. Collect weekly INR and prescribed Warfarin dosing.*					
	VerifyNow Aspirin Assay Laboratory Test	X *≤7 days pre-implant preferred*			X	X	X	X	X	X *If seen for bleeding or thrombotic complication*
	Enoxaparin bridging and GI Bleed									X *angiopoietin-2 levels if collected*

*Two abbreviated echos are performed in the operating room (OR): 1) TEE in OR after chest is open before going on cardio-pulmonary bypass, and 2) TEE in OR post-implant, after coming off cardio-pulmonary bypass, while chest is still open

** Diary includes Doppler pressure, presence of palpable pulse, LVAD parameters, and dizziness symptoms

Primary Objective	To characterize the 12-month overall major adverse event rate after the collective impact of Apogee standardized protocols and best practices. Major adverse events are defined to be occurrence of infection, bleeding, device malfunction, stroke or death.
[redacted]	[redacted]



C. Sponsor Contact Information

Sponsor contact information for the study is provided in **Table 1**. Study contact information can be provided separately since this information is subject to change throughout the conduct of the study. Periodic updates to study contact information will be provided to sites as needed.

Table 1: Sponsor Contact Information

US Study Contacts
Alejandra Gracia, Clinical Research Specialist Direct Phone: 1 (612) 242-6540 alejandra.m.gracia@medtronic.com Beth Ornell, Clinical Monitoring Manager Direct Phone: 1 (763)280-2332 beth.a.ornell@medtronic.com

D. Introduction

D.1. Background

Medtronic is sponsoring the Apogee study. Co-enrollment in Apogee is allowed for patients participating in the Destination Therapy (DT) Post Approval Study (PAS). Patients must be consented for the DT PAS to be eligible for participation in Apogee, which will require a separate consent.

Apogee is conducted within Medtronic's Product Surveillance Registry (PSR) platform and is specific under the DT PAS addendum. The Apogee addendum outlines data collection, applicable procedures, objectives, statistical methodology, analysis cohort, and reporting plans specific to the Apogee study which are not defined in the PSR core and MCS appendix (MCS PSR platform base protocol) or the DT PAS addendum. The combination of these elements together define the requirements for Apogee study.

E. Methodology

E.1. Study Design and Purpose

The Apogee study is a prospective, observational, multi-site study in Destination Therapy (DT) patients. The Apogee study includes three areas of data collection:

- Implant Procedure
- Blood Pressure Management
- Anti-coagulation / Anti-platelet Therapy

Sites choosing to participate in Apogee are expected to collect data in each of these three areas.

Most patients receiving mechanical circulatory support (MCS) experience severe adverse event burden. The 2013 Intermacs report showed that approximately 70% of patients experience a major adverse event within the first 12 months following LVAD implant, with major event defined as the first occurrence of infection, bleeding, device malfunction, stroke or death.[1]

Given the heavy adverse event burden, there is an opportunity to understand best practice guidelines. The purpose of Apogee is to further enhance scientific understanding of the implant procedure, optimized blood pressure management, and anticoagulation / antiplatelet therapies. The goals of Apogee are:

- To evaluate the collective impact of Apogee standardized guidelines and characterize impact on 12-month aggregate adverse event rate
- To better understand the effects of implant technique and patient management on clinical outcomes

E.2. Site Participation

It is expected that a subset of the DT PAS sites will participate in Apogee. DT PAS sites can choose to participate in Apogee, or they can decline Apogee and limit their participation to the DT PAS. As an estimate, if one-third of the approximately 50 DT PAS sites participate in Apogee, it is expected the Apogee cohort will be comprised of

1 Kirklin et al, Fifth INTERMACS annual report: Risk factor analysis from more than 6,000 mechanical circulatory support patients, J Heart Lung Transplant 2013;32:141-156

approximately (but not limited to) 100 patients from approximately (but not limited to) 17 Apogee sites. In general, it is expected that any site participating in Apogee would enroll all of their eligible patients in Apogee; however, there may be exceptions due to timing of Apogee activation, lack of patient interest, or concerns regarding non-compliance.

Prior to enrolling patients in Apogee, sites must be activated in the DT PAS and Apogee and have an established contract, Institutional Review Board (IRB) approval and fulfill any and all other Apogee or IRB initiation requirements. The consent for Apogee is separate from the DT PAS consent. The patient must be consented with the DT PAS consent prior to consenting with the Apogee consent. The study will be conducted in compliance with the protocol, Good Clinical Practice, and the applicable regulatory requirements. The clinical investigation shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

E.3. Enrollment and Duration

The enrollment duration of Apogee is expected to occur parallel to enrollment in the DT PAS. There are no additional inclusion or exclusion criteria to Apogee subjects outside of the requirements outlined in the MCS PSR platform base protocol and the DT PAS Addendum. Full enrollment is anticipated to require approximately 30 months from the date of first DT PAS enrollment and therefore with 12 months of follow-up, total study duration is expected to require 42 months. There is no minimum or maximum number of enrollments per site since data is being used for characterization purposes only.

Once consented with the Apogee consent, subjects are considered enrolled in Apogee and will be followed under the Apogee study for one-year post implant. After this, their participation in Apogee ends but subject will remain enrolled in DT PAS and will have follow-ups as outlined in the MCS PSR platform base protocol and DT PAS addendum.

F. Data Collection Schedule and Study Procedures

F.1. Data Collection Schedule

Apogee subjects will have scheduled follow-up assessments at 1 month, 3 month, 6 months, and 12 months post-implant or as prompted by reportable AEs, defined in the MCS PSR platform base protocol and the DT PAS addendum.

Apogee data collection is summarized in **Table 2** .

Table 2: Apogee Data Collection Table

		Enrollment	Baseline	Implant	Discharge	1M F/U	3M F/U	6M F/U	12M F/U	Unsch <12M
	Consent	**X**								
Implant Procedure	Detailed Implant Collection			**X**						
	Echo for 2D Velocimetry evaluation (digital image)		**X**	**X (2 TEEs*)**	**X** *With Lavare On x 5 min & Off x 5 min*		**X**			
	CT Scan Post-implant (digital image)			**X** *if performed*						
	Right Heart Cath (RHC) Hemodynamics		**X** *If subsequent RHC performed*	**X** *If performed*						
	Chest x-ray (digital image)			**X** Post-op						
	Videotape procedure			**X** *if obtained*						
BP	Patient BP Diary**				*Every morning ≥ 40 minutes after taking BP meds and while sitting. Collect whether HCP contacted for values out of range*					
	Medication BP Control				*Consider Medication Guidelines; Report Medication Changes*					
Anticoagulation/Antiplatelet	Home INR monitoring				*. Collect weekly INR and prescribed Warfarin dosing.*					
	VerifyNow Aspirin Assay Laboratory Test	X *≤7 days pre-implant preferred*			**X**	**X**	**X**	**X**	**X**	X *If seen for bleeding or thrombotic complication*
	Enoxaparin bridging and GI Bleed									**X** *angiopoietin-2 levels if collected*

*Two abbreviated echos are performed in the operating room (OR): 1) TEE in OR after chest is open before going on cardio-pulmonary bypass, and 2) TEE in OR post-implant, after coming off cardio-pulmonary bypass, while chest is still open
** Diary includes Doppler pressure, presence of palpable pulse, LVAD parameters, and dizziness symptoms

G. Implant Procedure Investigation

G.1. Implant Procedure Data Collection

Detailed information on the implant procedure will be collected, if available, including:

- Surgical incision and heparinization
- Arterial and venous cannulation, cardio-pulmonary bypass (CPB) time
- Inflow cannula and outflow graft placement
- Driveline placement and concomitant procedures
- Pump parameters exiting the OR
- Pericardium After Implant

G.2. 2-D Echo Color Doppler Velocimetry

Echos will be collected via digital media and uploaded to Medtronic via secure file transfer (e.g. Box). Medtronic will share echos with the vendor University of California San Diego (UCSD) so they can conduct 2D velocimetry evaluation using their proprietary software to evaluate flow in new ventricular imaging techniques.[2, 3, 4, 5, 6, 7, 8, 9, 10] The 2D echo color Doppler velocimetry (echo-CDV) modality allows for non-invasive personalized risk assessment of hemolysis and blood clot formation inside the left ventricle. It is hypothesized that this new modality can be used to non-invasively characterize the effect of left ventricular assist device support in LV hemodynamics in vivo leading to improved patient care.

The overarching goal is to evaluate the utility of echo-2D color Doppler velocimetry to guide LVAD positioning, pump settings, and minimize the risk for cerebrovascular accident (CVA), pump thrombosis (PT) and hemolysis in the clinical setting. The goals for this work are to:

- Evaluate shear stresses near cannula and their dependence on LVAD pump speed and cannula placement (assess how to minimize hemolysis risk)
- Evaluate changes in blood transport efficiency and blood stasis as a consequence of LVAD placement (assess how to minimize stasis and risk of thrombus formation)
- Evaluate energetic and momentum efficiency created by flow patterns (e.g. flywheel effect) as a potential outcome predictor

Echocardiograms will be obtained when performed per standard institutional procedures, which is expected to occur at the following timepoints:

- Baseline (prior to implant) – transthoracic echocardiogram (TTE)
- In OR, after chest is open prior to cardio-pulmonary bypass and prior to implantation - transesophageal Echocardiogram (TEE)
- In OR, after implantation, off cardio-pulmonary bypass, while chest is still open- transesophageal Echocardiogram (TEE)
- Prior to Discharge (capture with Lavare off for 5 minutes*)- transthoracic echocardiogram (TTE)
- Prior to Discharge (capture with Lavare turned on for 5 minutes*)- transthoracic echocardiogram (TTE)
- 3 months post-implant - transthoracic echocardiogram (TTE)

Echo data will also be collected on a Case Report Form (CRF).

2 Braun et al, Non-Invasive Mapping of Intraventricular Flow Patterns in Patients Treated with Left Ventricular Assist Devices. Journal of Cardiac Failure, Supp 24, Vol. 23 No. 8S August 2017
3 Garcia, del Alamo et al, IEEE TransMedImag. 2010
4 Hendababi et al Ann Biomed. Eng. 2013
5 Bermejo et al, Am J Physiology 2014
6 Martinez-Legazpi et al, JACC 2014
7 Wong et al, J Biomech 2014
8 Rossini et al, J Biomech 2016
9 Rossini et al, Meccanica 2016.
10 Martinez-Legazpi et al JACC Img. 2017. US patent (pending) #15/360,783

*The echo at Discharge should also capture images with Lavare on and off (capture basic views with Lavare turned OFF for 5 minutes, then doing the views needed for Doppler velocimetry with Lavare ON for 5 minutes to see the improved washing with Lavare turned on). Lavare views should:

- Evaluate shear stress near cannula
- Evaluate changes in blood transport efficiency and blood stasis
- Evaluate energetic and momentum efficiency created by flow patterns (e.g. flywheel effect)

For instructions on the echo image capture, please reference the most recent version of the Apogee Echocardiography Manual.

G.3. Chest X-Ray (if performed)

A digital image of the standard post-op chest x-ray (expected to occur on Post-op Day 1) will be collected and uploaded to Medtronic.

G.4. CT Scan (if performed)

If a CT scan is performed post implant, a digital image will be uploaded to Medtronic.

G.5. Right Heart Catheterization (RHC) Hemodynamics Collection (if performed)

If a subject undergoes any RHC during the first year post-implant, information about right ventricular function will be collected on the CRF, as well as any available baseline data from a previous RHC prior to implant.

G.6. Videotape Procedure (if performed)

A videotape of the procedure will be collected for any sites with capability and interest to videotape the procedure for training purposes, if performed. If the procedure will be videotaped, the recording will follow institutional procedure and must be specified in the subject's signed consent. The recording is recommended to capture the apical implant portion, including the cannulation sequence and aortic outflow anastomosis.

H. Blood Pressure (BP) Management Investigation

Apogee sites will manage blood pressure according to blood pressure management guidelines described in the DT PAS PSR platform addendum and the product labeling, which may include but is not limited to the IFU and the product reference manuals. In addition, Apogee sites will report items from the patient diary and consider medication guidelines for hypertensive patients. The patient will check whether they have a palpable pulse at each check. Diary recordings will be entered into the CRF, including Doppler pressure, presence of palpable pulse, LVAD measurements and presence of dizziness.

Inpatient Medication Guidelines
1. Manage to target goal: 75-90 mmHg (via Doppler/cuff method once arterial line pulled) 2. Ensure patient and caregiver(s) properly trained on Doppler/cuff method prior to discharge 3. Medication guideline recommendations for management of hypertensive patients prior to discharge: <u>In patients without AKI or significant renal dysfunction:</u> • First line therapy: Angiotensin converting enzyme inhibitor (ACE-I) or Angiotensin II receptor blocker (ARB)

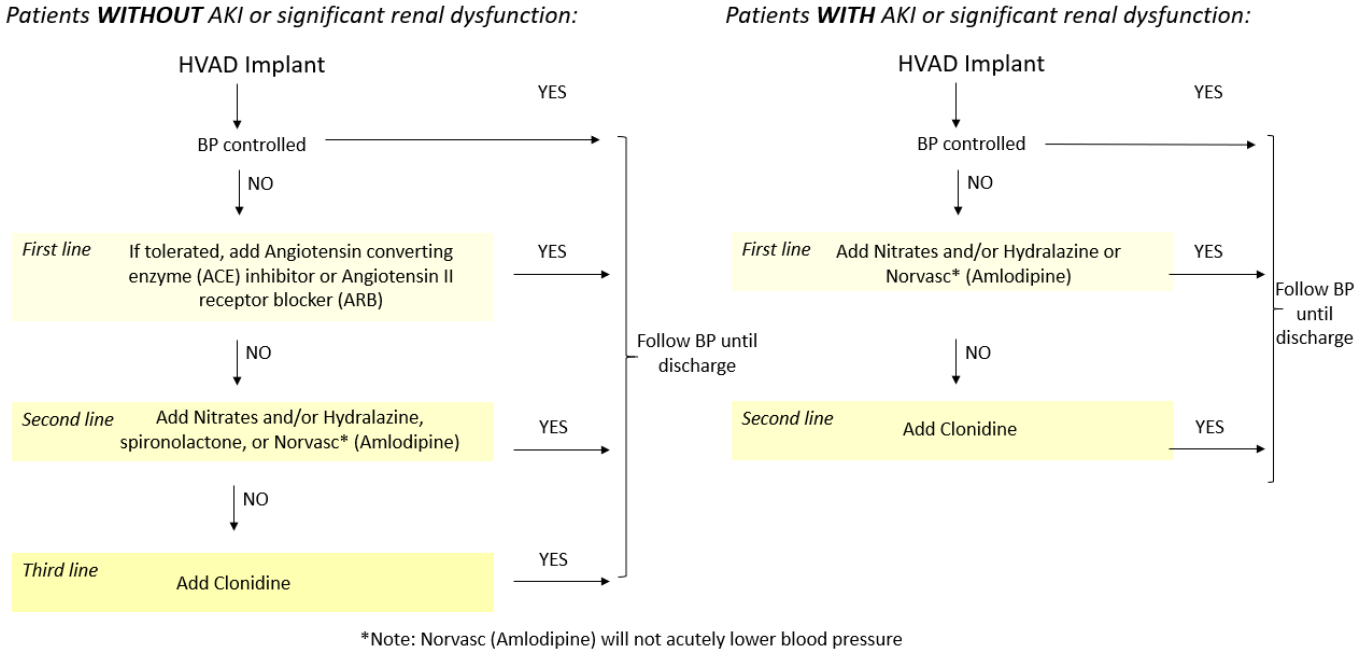
- Second line therapy: Nitrates and/or Hydralazine, spironolactone, or Norvasc* (Amlodipine)
- Third line therapy: Clonidine

<u>In patients with AKI or significant renal dysfunction:</u>

- First line therapy: Nitrates and/or Hydralazine or Norvasc* (Amlodipine)
- Second line therapy: Clonidine

*Note: Norvasc (Amlodipine) will not acutely lower blood pressure

In-patient Blood Pressure Management Algorithm



*Note: Norvasc (Amlodipine) will not acutely lower blood pressure

Outpatient Diary Collection & Medication Guidelines

Blood pressure monitoring (using Doppler with cuff)

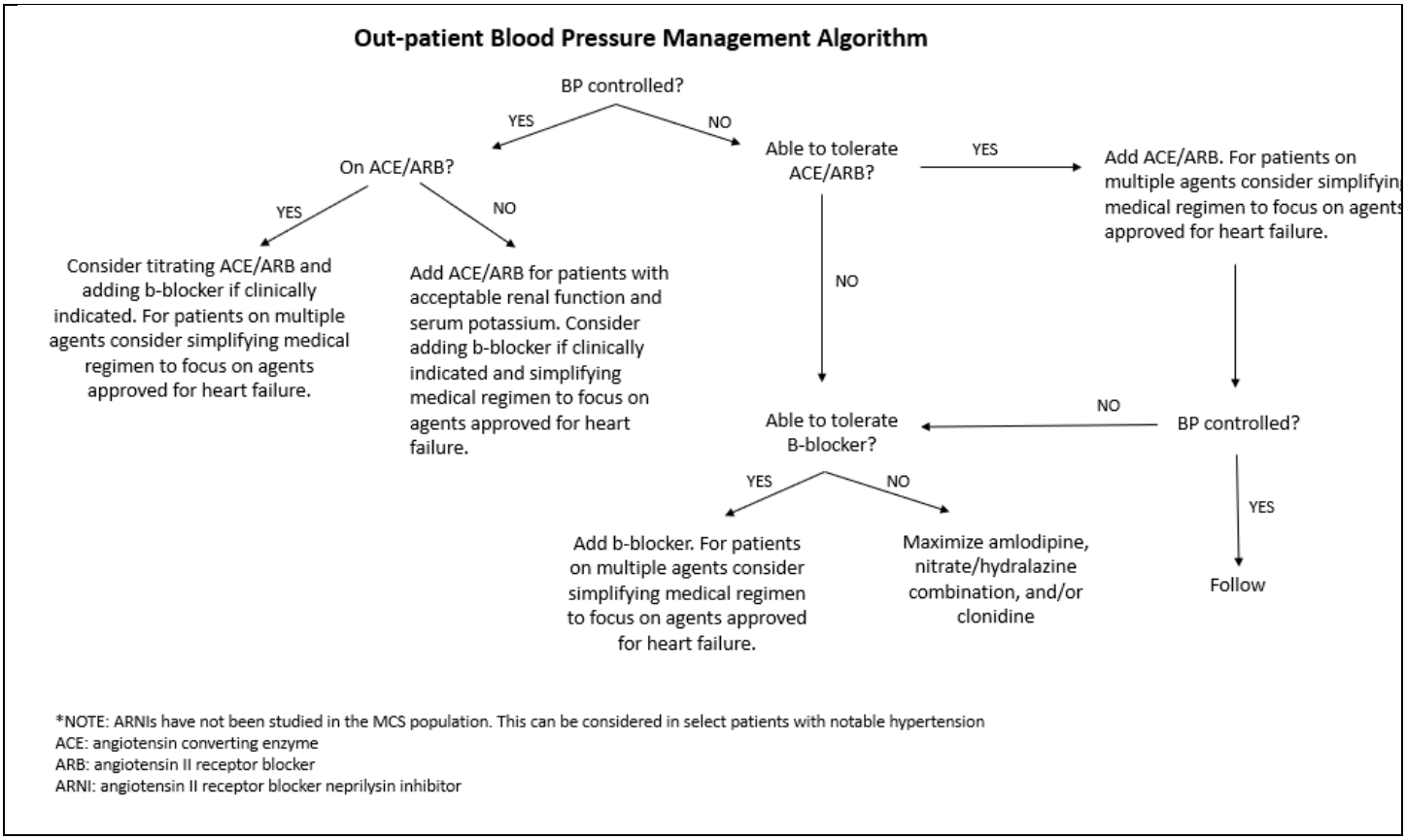
- Time of day: Measure every morning at least 40 minutes AFTER taking BP medication and during resting conditions, while sitting
- Frequency: Measure daily. If stable after 1 month of daily monitoring, Investigator can consider reducing frequency to measuring 3 times per week (e.g., every Monday/Wednesday/Friday schedule). Stable is defined as: no instances of BP>90 mmHg for three consecutive days and not a single occurrence of BP>110 mmHg (i.e. no instances of needing to call HCP)
- Diary: Patient to record Doppler pressure, presence of palpable pulse or dizziness, and HVAD measurements from controller (i.e. power, flow, RPM, peak, trough) in diary and bring to site during scheduled visits. Site will record these onto CRF.

Patient should call site if:

- BP >90 for 3 consecutive days or if postural symptoms >48 hours (e.g. orthostatic reaction)
- BP >110 for single timepoint (take BP measurement twice before calling to confirm both show >110 at timepoint)
- BP <60 for single timepoint (take BP measurement twice before calling to confirm both show <60 at timepoint)
- Patients with symptoms of hypotension (dizziness/syncope/presyncope/weakness) should be instructed to call even if values read normal.

Medication guidelines for hypertensive patients post discharge

- See algorithm



I. Anti-Coagulation / Platelet Therapy Investigation

I.1. Aspirin Management Plan

The site will be asked to report the patient's aspirin dose and dose start date at discharge and throughout follow-up or when the patient presents with a bleeding or thrombotic event, including hemorrhagic or ischemic strokes. Per the HeartWare HVAD System Instructions for Use, "In general, aspirin should be started at doses >81 mg/day" (i.e., moderate-dose aspirin of 162mg or high-dose of 325mg, etc.). The Medication Log captures aspirin dose and any changes.

I.2. VerifyNow Aspirin Assay Laboratory Test

A VerifyNow Aspirin Assay and CBC (if available) will be collected along with the current aspirin dose and its start date at each scheduled follow-up visit through 12 months. The assay and CBC (if available) will also be collected at all Unscheduled Visits, if the patient presents with a bleeding or thrombotic complication, including hemorrhagic or ischemic strokes. See Appendix A for instructions on the use of the VerifyNow Aspirin assay, which is also available online at http://www.accumetrics.com/products/verifynow-system-platelet-reactivity-test.

The purpose of collecting this information is to correlate the VerifyNow Assay results with bleeding or thrombotic events. Information from the assay collection may characterize the platelet reactivity and responsiveness to aspirin in patients supported by the HeartWare HVAD System, up to one-year post-implant. It may also characterize whether platelet activity is greater in ventricular assist device (VAD) patients with frequent/severe thrombotic events as compared to those with less frequent/less severe thrombotic events, and

also whether levels of platelet activity/reactivity are reduced in VAD patients with hemorrhagic events compared to those without such events.

During this study, sites should continue to follow their current institutional practice and IFU recommendations for aspirin dose adjustments. Test results from the VerifyNow Assay should not be used to guide aspirin dosing unless this is the center's current standard of practice.

I.3. Home INR Monitoring

The HVAD IFU recommends anticoagulation with the recommended INR range of 2.0 – 3.0. Home INR monitoring will be instituted with point of care testing for subjects on anticoagulation therapy with intent to improve time in therapeutic range. Where possible, INR monitoring equipment will be provided to subjects for weekly INR monitoring. Sites will record reported INR values.

The anticoagulation management strategy/protocol will be site defined. Sites should use a warfarin management software as part of the dosing algorithm (sites can follow their VAD center protocol and manage warfarin dosing using their preferred software algorithms). Any suspected stroke should be confirmed with CT scan.

I.4. Enoxaparin Bridging Recommendation (for stable ambulatory patients with sub-therapeutic INR)

It is recommended that ambulatory patients with an INR ≤ 1.7 be bridged with enoxaparin (or fondaparinux) unless contraindicated, such as increased risk of bleeding. Details of data collection and enoxaparin bridging recommendations include:

- Collect previous history of gastrointestinal (GI) bleeding, presence of nasal arteriovenous malformation (AVM), proton pump inhibitor (PPI) use, bleeding location (upper/ lower / small bowel bleed), and any endoscopic procedure(s) findings such as video capsule endoscopy (VCE) and enteroscopy
- Enoxaparin Dosing: For eGFR > 30 -- 1mg per kg bid rounded to the nearest 10mg
- Dosing may be altered for patients with increased risk of bleeding where half-dose dosing may be considered (0.5mg/kg)
- A patient should meet the following criteria to receive enoxaparin bridging:
  - Minimum weight: women must weigh more than 45 kg; men more than 57 kg
  - Most recent platelet count > 100,000/UL
  - Ability to safely and accurately self-administer enoxaparin
- In a patient with a contraindication to enoxaparin, fondaparinux can be utilized:
  - Fondaparinux 7.5mg SC daily (wt 50-100kg)
  - Fondaparinux 10mg SC daily (wt > 100mg)

I.5. GI bleeding Recommendation

Subject management strategies for GI bleeding (GIB) have recently been described, including an endoscopic algorithm to eliminate sequential and overlapping procedures, and to eliminate low-yield procedures;.[11]This algorithm was focused on maximizing procedures with the highest diagnostic and therapeutic yields while

11 Axelrad et al, Limited usefulness of endoscopic evaluation in patients with continuous-flow left ventricular assist devices and gastrointestinal bleeding. J Heart Lung Transplant 2018;37:723–732

minimizing low-yield procedures or procedures without therapeutic potential. **Table 3** shows the recommended algorithm, adapted from Axelrad 2018 et al.[11]

Table 3: Proposed endoscopic algorithm for the management of GIB[11]

	If Upper GI Bleed Source Suspected	If Lower GI Bleed Source Suspected	If Occult GI Bleed
Signs / Symptoms	Melena, coffee-ground emesis, hematemesis	Hematochezia	Hemepositive brown stool, iron deficiency anemia
Suggested Actions	Push Enteroscopy (PE) as first endoscopic procedure rather than EGD with sequential push enteroscopy	Colonoscopy	• Initial medical management with blood products • and/ or temporary reduction or withholding of anti-thrombotic therapy followed by push enteroscopy if major bleeding occurs as defined by the replacement of >2 units of pRBC over a 48-hour period
	For all patients, propose further endoscopic evaluation for: • Hemodynamic instability or continued GIB despite administration of blood products • Persistent GIB despite withholding or after resumption of lower dose anti-thrombotic therapies • Age-appropriate colon cancer screening		

Diagnostic testing for GI bleeds will be collected. If acquired by the center due to recurrent GI bleeding, angiopoietin-2 levels will be collected.

J. Objectives and Statistical Methodology

General Considerations

Many ancillary objectives are not statistical in nature. Ancillary objective analysis methods will be detailed in the Apogee Statistical Analysis Plan. This is an observational study; therefore, no hypothesis tests are planned.

The Apogee study might observe variations in data collection due to 1) variations in routine care practices across participating sites and 2) the COVID-19 pandemic. Apogee does not have statistical hypotheses; thus, available data will be analyzed.

J.1. Primary Apogee Objective

To characterize the 12-month overall major adverse event rate after the collective impact of Apogee standardized protocols and best practices. Major adverse events are defined to be occurrence of infection, bleeding, device malfunction, stroke or death.

Endpoint Definition

Events counted as "major adverse events" are:

- Major infection as defined by Intermacs adverse events V5
- Major bleeding as defined by Adverse Events
- Device Malfunction as defined by Adverse Events
- Any stroke (includes ischemic stroke, acute symptomatic ICH, and clinically covert ischemic stroke or ICH) as defined by Adverse Events as a sub-category of neurological dysfunction
- All-cause death

Analysis Methods

Time to first major adverse event will be analyzed using Kaplan-Meier methods, with Time 0 being exit from the operating room following implant. Subjects will be censored upon the earliest of explant of the original device, study exit, last known follow-up, and the date of their 12-month follow-up. There is no planned formal comparison of the major AE rate, though it could be informally compared to results from other studies, or non-Apogee subjects in DT PAS.

Additionally, the individual types of major adverse events will be summarized.

Only DT PAS subjects successfully implanted with the HeartWare HVAD and enrolled in the Apogee Study will be included in this analysis.

J.2. [redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

- [redacted]

J.3. [redacted]

- [redacted]

J.4. [redacted]

- [redacted]

K. Sample Size Considerations

No minimum or maximum sample size will be specified since objectives are characterizations only and intended for hypothesis-generating purposes.

L. Report and Analysis Schedule

A final report will be sent to sites at the conclusion of the study with a summary of study results.

M. Addendum Version History

Version	Version Date	Summary of Changes & Rationale	Author(s)/Title
1	27 Jul 2018	Initial Release	Verla Laager, Sr. Clinical Program Manager
2	01 Dec 2020	General administrative changes throughout the document: • Added MCS PSR platform base protocol and DT PAS addendum references and clarifications regarding the names of the protocols • Added table of contents, updated glossary, expanded abbreviations as appropriate and other minor editorial modifications, clarifications, and reformatting • Updated the synopsis to reflect updates to addendum Replaced Intermacs V3.0 adverse event terminology throughout the document to Intermacs V5.0 to align with DT PAS Addendum Section C- Updated Table 1 with updated contact information Section E.2 – Included clarification that Apogee cohort approximation is not limited to 100 patients Updated addendum to align with modifications in the MCS PSR platform base protocol and DT PAS addendum including: • Section E.2 – Updated number of sites from 55 to approximately 50, as stated in DT PAS addendum • Section E.3 – Update in the anticipated time to achieve full enrollment duration • Section F.1. – Included follow-up assessment • Section H – Replaced HVAD IFU with “product labeling, which may include but is not limited to the IFU and the product reference manuals” Section G.1 – Added clarifications and rewording for clarity and removed section under 2D color velocimetry since it is included in the Apogee Echocardiography Manual, which is a separate document Section J.4 – Added section to describe known or foreseeable factors that may compromise study outcomes to fulfill ISO14155:2020 requirement Section M – New section to include addendum version history	Alejandra Gracia, Clinical Research Specialist

APPENDIX A: VerifyNow Aspirin Assay: Sample Preparation

The VerifyNow Aspirin Test Procedure should be performed according to manufacturer's instructions provided below:

Verify*Now*® Aspirin Test Procedure

Principle

Aspirin affects platelet function by irreversibly inhibiting the cyclooxygenase-1 (COX-1) enzyme involved in the conversion of arachidonic acid to thromboxane A2, which ultimately activates the GPIIb/IIIa receptors involved in platelet aggregation. If aspirin has produced the expected anti-platelet effect, such aggregation will not occur. The Verify*Now* Aspirin Test incorporates the agonist arachidonic acid to activate platelets. The Aspirin Test is designed to measure platelet function based upon the ability of activated platelets to bind fibrinogen. Fibrinogen-coated microparticles aggregate in whole blood in proportion to the number of unblocked platelet GP IIb/IIIa receptors. Light transmittance increases as activated platelets bind and aggregate fibrinogen-coated beads. The instrument measures this change in optical signal caused by aggregation.

Materials Required

- VerifyNow Instrument with Electronic Quality Control (EQC).
- VerifyNow Aspirin Test Device (reagent device), 10 (PN: 85053-10) or 25 (PN: 85053), individually sealed in foil pouches. Each test device contains lyophilized fibrinogen-coated beads, platelet agonist, peptide, bovine serum albumin, stabilizer, and buffer.
- Store test devices at 2°C to 25°C (36°-77°F) Store at room temperature.
- Greiner Bio-One Vacuette® 2ml blood collection tubes containing 3.2% sodium citrate. Greiner Catalog # 454322 or Nipro catalog #NP-CW0185-1 blood collection tube (1.8ml) containing Sodium Citrate (3.2%).
- Phlebotomy supplies, including needle of 21 gauge or larger.
- Wet Quality Control (VerifyNow Assay WQC), P/N 85047, Box of 6 Diluent Tubes and 6 Pellets. QC materials are stable at room temperature until the expiration date indicated on the tube or pellet container.

Specimen Collection and Specifications

Specimen Type: Whole blood collected from venous or arterial sites must be collected in or immediately transferred to Greiner 2.0 mL partial fill blue top tubes containing 3.2% Sodium Citrate. The tube must be filled to its intended whole blood capacity (indicated by small black line).

- Samples should be collected between 2 and 30 hours after ingestion of aspirin.
- Blood must set a minimum of 30 minutes after collection before test but no longer than 4 hours.

Instructions for Sample Collection Directly Into Vacuum Collection Tubes:

1. Whole blood may be collected from venous or arterial sites using a 21 gauge or larger needle in partial fill 3.2% citrate vacuum collection tube. Blood samples should be obtained from an extremity free of peripheral venous infusions.
2. Perform the phlebotomy and obtain the appropriate volume of blood in the sample tube following a discard tube of at least 2 mL of whole blood. DO NOT DRAW A SAMPLE FOR ANY PLATELET FUNCTION TEST AFTER A TUBE THAT CONTAINS EDTA (PURPLE TOP). Always draw the sample tube(s) for the Verify*Now* Test first.
3. Gently invert the citrated tube containing whole blood 5 times immediately after collection to mix the blood with the anticoagulant and prevent clotting.
4. Samples must be kept at room temperature. Do not refrigerate, freeze or centrifuge the samples to be used for the Verify*Now* Test.

5. Samples that are difficult to obtain may hemolyze or clot. Samples that are hemolyzed or clotted should be recollected.

Special Instructions if blood is obtained from an indwelling catheter:

1. Whole blood samples that are obtained from an indwelling catheter should be collected after sufficient discard (approximately 5 mL) has been drawn to clear the line.
2. Ensure indwelling catheter is free of clots.
3. When using a syringe, transfer blood to the appropriate blood collection tube **immediately** after collection.
4. Immediately gently invert the citrated tube containing whole blood at least 5 times to mix the blood with the anticoagulant and prevent clotting.
5. Samples must be kept at room temperature. Do not refrigerate, freeze or centrifuge the samples to be used for the Verify*Now* Test.
6. Samples that are difficult to obtain may hemolyze or clot. Samples that are hemolyzed or clotted should be recollected.

***Sample Stability and Storage*:** The sample must be incubated at room temperature for 30 minutes prior to testing and can be used up to 4 hours after collection if stored at room temperature (18 to 25 °C). *Do not refrigerate or freeze specimen*.

***Sample Precautions*:** Collection of the blood specimen should be performed with care to avoid hemolysis or contamination by tissue fluids. Samples with evidence of clotting must not be used.

***Interfering Substances*:**

Laboratory testing was performed to determine the effects of several classes of drugs on VerifyNow Aspirin Test results. The following medications may cause a change in platelet function. The following information should be considered for patients who are to be tested with the VerifyNow Aspirin Test.

P2Y12 Inhibitors: Plavix®, Ticlid ®, and Effient® are commonly prescribed in conjunction with aspirin. While infrequent, these agents may cause a reduction of ARU in some patients. However, the effect of the P2Y12 inhibitors did not affect the categorization of patients taking aspirin as having platelet dysfunction (i.e. ARU < 550) due to aspirin ingestion. The duration of inhibitory effects varies among these P2Y12 inhibitors. Average durations are listed below:

- Plavix (up to 5 Days)
- Ticlid (up to 5 Days)
- Effient (up to 10 days)

Other Anti-Platelet Agents: These agents can all inhibit platelet function and may result in a decreased ARU value independent of the effects of aspirin. The duration of inhibitory effects varies among drugs. Average duration times are listed for each drug.

- Aggrenox (10 days)
- Persantine (12 hours)
- Pletal/Cilostazol (12 hours)

NSAIDs: Like aspirin (ASA), NSAIDs have been documented to inhibit platelet function. Unlike ASA, NSAIDs do not irreversibly inhibit platelet function. This may lead to less platelet inhibition by ASA if the NSAID and ASA are taken at the same time. Average duration times for these inhibitory effects are given for each drug.

- Ibuprofen (Motrin, Advil) (8 hours)

- Naproxen (Aleve, Anaprox, Naprelan, Naprosyn) (24 hours)
- Diclofenac (Voltaren, Cataflam) (24 hours)
- Indocin (24 hours)
- Feldene (50 hours)

GP IIb/IIIa Inhibitors: Patients who have been administered tirofiban (Aggrastat®) or eptifibatide (Integrilin®) within two days, or abciximab (ReoPro®) within two weeks should not be tested.

Other classes of commonly used drugs were tested with no significant effect on VerifyNow Aspirin Test performance (antioxidants, ACE inhibitors, antiarrhythmics, anticoagulants, antidepressants, insulin, allopurinol, alcohol, beta blockers, bronchodilators, calcium channel blockers, gastrointestinal medications, betamethasone, lovastatin, and the thyroid hormone L-thyroxine). The thrombolytic agent streptokinase showed a measurable inhibition of platelet function, as measured by the VerifyNow Aspirin Test.

Laboratory and clinical testing was performed to assess the effect of the levels of several blood constituents:

Test performance was not affected by hematocrit values between 29-56%, platelet count values of ≥ 92,000 platelets per microliter or moderate to extensive blood hemolysis induced by physical manipulation. The degree of hemolysis was determined by visual examination of plasma from centrifuged samples collected concurrently with VerifyNow Aspirin Test samples.

No significant interference was observed on samples studied with triglyceride concentrations up to 577 mg/dL.

Fibrinogen levels between 164-529 mg/dL were tested with the VerifyNow Aspirin Test. No known relationship exists between performance of VerifyNow Aspirin Test and fibrinogen levels.

Handling Conditions

The sample must be incubated for 30 minutes at room temperature prior to testing. If testing is delayed, the sample can be stored at room temperature (18 to 25 °C) for up to 4 hours. *Do not refrigerate or freeze specimen*. The sample must be handled in accordance with all policies and procedures relating to the collection, processing and disposal of biohazardous samples.

Reagent Storage and Handling
Reagents Required:

1. All required reagents are contained within the individually packaged VerifyNow Aspirin Test device. Each test device contains lyophilized fibrinogen-coated beads, platelet agonist, peptide, bovine serum albumin, stabilizer, and buffer.
2. Each individually sealed test device contains the lot number and expiration date stamped on the foil pouch.
3. Once removed from its foil pouch, the test device must be handled only by the finger grip and used immediately.

Receipt of Shipment:

1. When a shipment of kits is opened, check the temperature indicator located on the outside of the box. If the temperature indicator is activated, this indicates exposure to elevated temperatures and a VerifyNow Level 2 WQC should be performed.
2. If the Level 2 WQC result does not fall within the accepted range on the package insert, call Accumetrics Technical Support at (800) 643-1640.

***Storage Temperature*:**

1. Store Test Devices at 2° C to 25° C (36° - 77° F).

2. If refrigerated, allow test devices to reach room temperature, 18° C to 25° C (64° -77° F), prior to use.
3. **Test devices should remain sealed in the foil pouch until ready for use to prevent damage by humidity.**

***Reagent Quality Control*:**

1. The manufacturer recommends that a Level 2 WQC be run once each time a new lot or a new shipment of VerifyNow Aspirin Test kits is received. A Level 2 Quality Control should also be performed on each lot of test devices whenever a problem is suspected with the temperature indicator of a newly received lot of test devices.
2. Level 1 and Level 2 Quality Control must also be performed at the frequency specified. Please refer to the Quality Control section below for additional instructions.

Calibration and Calibration Verification

1. The Verify*Now* Aspirin Test devices are calibrated by the manufacturer at the factory. This calibration information is contained in the barcode on the pouch of each test device.
2. The barcode must be scanned whenever a new lot of test devices is to be tested. The system will not allow a test device to proceed without the lot number calibration information entered into the system. If a new lot of test devices is being used, the instrument will prompt the user by displaying a barcode icon after the test device is inserted.
    a. At prompt, place the test device pouch approximately one inch in front of the barcode reader found on the left side of the instrument, so that the light shines on the center of the barcode.
    b. An audible beep will be heard when the instrument receives the required information.
    c. The user needs only to perform this action once per lot.
3. No additional calibration is performed by the user.
4. Calibration verification is performed by the use of WQC materials with every new lot of reagent and at specified time intervals, with periodic review of QC results by the laboratory technical supervisor. Tests of platelet reactivity are non-linear, and no additional calibration verification is required.

Quality Control Procedures

***Electronic Quality Control*:** The Electronic Quality Control Device (EQC) is supplied with each instrument and must be run each day of use prior to reporting patient results. This device verifies instrument optics, reagent mixing and instrument pneumatics. Refer to the Verify*Now* System User Manual for additional information.

1. If required, enter Operator ID and Password.
2. The EQC Device is located in a storage port on the right side of the instrument.
3. Choose QC by pressing the QC button from the main screen.
4. Open instrument cover. Remove the EQC Device from the storage port, open instrument cover and insert the EQC Device into the instrument. Close instrument cover.
5. EQC will automatically run.
6. Open instrument cover and remove the EQC Device and return it to the storage port. Close instrument cover. A result of PASS or FAIL will be displayed.
7. If the EQC Device result is “FAIL”, repeat the EQC. If the result is “PASS”, continue with patient testing. If the EQC result is “FAIL” after the second analysis, use the cleaning cartridge as described in the Maintenance Section below and rerun the EQC.
8. Print result and keep as source document.

***Wet Quality Control*:** The manufacturer recommends that a Level 2 WQC be run once each time a new lot or a new shipment of Verify*Now* Aspirin Test kits is received. The Wet Quality Control (WQC) procedure must also be performed whenever a problem is suspected with the temperature indicator of a newly received lot of test devices, whenever a problem is suspected with the Verify*Now* System, and as part of the laboratory quality control program.

Sample Preparation:

1. All control material should be stored at room temperature (18 to 30 °C).
2. Do not open the vial containing the Level 2 Control pellet until immediately prior to use.
3. Control Level 1 is ready for use as provided.

Wet Quality Control:

1. If required, enter Operator ID and Password.
2. Press the QC Icon key. The *Insert Cartridge* screen will display.
3. Open the foil pouch and remove the test device. The test device should only be handled by the finger grip.
4. Remove the protective sheath from the test device needle by pulling directly up on the sheath. Do not twist the sheath as this may remove the needle.
5. Open instrument cover. Insert the test device at the instrument prompt. If this is a new device lot, the Bar Code prompt will display. At prompt, place the test device pouch approximately one inch in front of the barcode reader found on the left side of the instrument, so that the light shines on the center of the barcode. An audible beep will signal that the instrument has read the bar code, and the testing will continue.
6. Prepare the WQC Sample.
    a. Level 1: Test Control Level 1 is ready for use as provided.
    b. Level 2: Remove the stopper from the tube containing the Level 2 Control diluent by twisting and pulling the cap simultaneously.
    c. Add the Level 2 control pellet to the Level 2 control diluent tube and replace the stopper by pressing and turning simultaneously.
    d. Invert the tube gently 5 times to mix.
7. At the prompt, insert the sample onto the device needle. Close instrument cover. The test will automatically begin. **CAUTION**: The sample is under pressure once it is inserted onto the device needle. DO NOT REMOVE the test device or control tube from the instrument until the test is completed.
8. The instrument will run the test and display the result.
9. Print or record the result and return to the Main Screen.
10. Open instrument cover. Remove the test device by grasping the device finger grip and pulling straight up. Do not remove the sample or diluent tube from the device. Close instrument cover.
11. Discard the used device and quality control tube as biohazardous waste.
12. The instrument is ready to test the next sample.
13. Determine that the WQC result is within the acceptable range of values printed on the test device pouch provided with the test.
14. If the WQC is in control, proceed with the test of patient samples. If the WQC is out of range, follow the procedure established by your institution.
15. Print result and keep as source document.

***System (Internal) Quality Control for Each Sample Tested*:**

1. Each time a test device is run on the Verify*Now* System, the instrument verifies the test device expiration date, sample filling, optics performance, correct fluid transfer, and proper mixing.
2. The system controls prevent the operator from running an expired test device.
3. The system also detects certain other operator errors, such as placing the test device or the sample in the instrument at the wrong time, or removing the test device before the test is complete. These controls prevent reporting of an inaccurate test result.
4. The test device internal controls in the Verify*Now* Aspirin Test device can detect failures of the reagent system due to improper storage or handling conditions.

5. The internal controls will flag an improperly collected or mishandled blood sample, or a blood sample with certain types of interfering substances.
6. The test device internal controls detect errors from the reagent system, adverse environmental conditions, and additional types of operator errors.

R*ECALL OF EQC OR WQC RESULTS*:

1. The last 100 EQC and WQC results can be recalled at any time. You may scroll by using the arrow keys on the keypad.
2. Press the Maintenance button from the Main Screen.
3. Press the Next arrow 3 times to advance to the Maintenance Submenu where folders are displayed with the words EQC (2nd button) and WQC (3rd button).
4. Press the appropriate button to recall the EQC or WQC results.
5. Press the back arrow to return to the Main Screen.

Testing Patient Samples

1. Refer to the VerifyNow System User Manual for complete operating instructions.
2. Power on the instrument. This will initiate the following startup checks:
    a. A system program and data memory check to ensure memory integrity;
    b. A system temperature check to ensure the test device warming plate reaches and maintains the proper temperature;
    c. A system check of proper operating voltages; and
    d. A system intra-communication validation.
3. Perform Electronic Quality Control if one has not been performed within the required timeframe. The following checks are performed:
    a. Instrument optics.
    b. Pneumatics system that draws the sample into the test device and moves it into the test device for reaction and measurement.
    c. Reagent mixing parameters and sample data acquisition.
    d. Correct calibration parameters.
4. If required, enter Operator ID and Password.
5. If required, enter the Patient ID.
6. Open the foil pouch and remove the test device. Test devices should only be handled by the finger grip.
7. Remove the needle's protective sheath by pulling directly up on the sheath. Do not twist the sheath as this may remove the needle.
8. Open instrument cover. Insert the test device at the instrument prompt. If this is a new device lot, the Bar Code prompt will display. At prompt, place the test device pouch approximately one inch in front of the barcode reader found on the left side of the instrument, so that the light shines on the center of the barcode. An audible beep will signal that the instrument has read the bar code, and the test will continue.
9. At the instrument prompt, invert the sample tube at least 5 times, and insert onto the needle in the test device. Close instrument cover. CAUTION: Sample is under pressure. Do not remove sample tube from test device. Only remove test device from the instrument after the test is completed.
10. The instrument will run the test and display the result in less than five minutes.
11. Record or print the sample result.
12. Open instrument cover. Remove the test device by grasping the device finger grip and pulling straight up. Do not remove the tube from the test device. Close instrument cover.
13. Dispose of the entire test device/sample tube in appropriate biohazard waste container.
14. The instrument is ready to test the next sample.

Recall Patient Results: In order to enable the recall of specific patient results, the instrument must be configured to require a Patient ID to be entered before each test device is performed.

1. If required, enter Operator ID and Password.
2. CHOOSE THE SECOND OPTION (BUTTON NEXT TO FILE FOLDER) FROM THE MAIN SCREEN.
3. Enter the Patient ID, and press the arrow for Next.
4. An Aspirin Test result is indicated by an "a".
5. Record or print the results. The most recent result is displayed, along with the date stamp indicating the date and time the test was performed. To toggle to other results, use the left and right arrow key.
6. If you choose the PRINT ALL icon, everything displayed below the blinking cursor will print.

Reported Results

Test results are reported as Aspirin Reaction Units (ARU), which are calculated as a function of the rate of aggregation. Interpretation of results is based on the following assigned cutoffs:

Interpretation of Results:

≥550 ARU - Platelet dysfunction consistent with aspirin has not been detected

< 550 ARU - Platelet dysfunction consistent with aspirin has been detected

Results should be interpreted in conjunction with other laboratory and clinical data available to the clinician.

Reference Range:

The reference range for pre-aspirin samples is 620-672 ARU.

Test Limitations and Method Notes

1. To minimize problems during specimen handling, test performance and reporting of test results, the area where testing is performed must contain the proper workbench space, ventilation, utilities, and supplies necessary for conducting the type and volume of testing performed.
2. Place the VerifyNow instrument on a clean, firm, level bench top, which is free of excessive vibration from equipment such as a centrifuge. Provide adequate space around the instrument to access instrument components and be sure the area is free from exposure to unusual temperature fluctuations.
3. Do not locate the VerifyNow instrument in an area next to a source of heat, air conditioning or in direct sunlight. Do not place the instrument under an incandescent light source.
4. The VerifyNow instrument operates at ambient temperature (18-32°C or 64-90°F) and up to 85% humidity without condensation.
5. The lyophilized agent is hygroscopic and can degrade after prolonged exposure to room air. Therefore, the test device should be used shortly after removal from the foil pouch.
6. Store reagents and quality control material according to the package directions. The test devices can be stored either at room temperature or in the refrigerator.
7. Delays in testing or difficulty of specimen collection may result in spurious values. Do not test any sample that is clotted, too old, hemolyzed or that has been mishandled or mislabeled.
8. When results are not within the expected limits, the possibility of improper sample collection or handling should be investigated. Repeat the test using a new test device and sample.

9. Patients with inherited platelet disorders such as von Willebrand Factor Deficiency, Glanzmann Thrombasthenia and Bernard-Soulier Syndrome have not been studied with the VerifyNow Aspirin Test.
10. Patients receiving the following anti-platelet agents may not be tested with VerifyNow Aspirin Test, based on documented interference testing results: GPIIb/IIIa inhibitors, dipyridamole, clopidogrel, non-steroidal anti-inflammatory drugs (NSAIDS) which inhibit COX-1 and/or COX-1, COX-2 enzymes (ibuprofen, naproxen, diclofenac, indomethacin, and piroxicam).
11. The performance of VerifyNow Aspirin Test on patients with acquired non-drug induced platelet abnormalities is not known.
12. The performance of VerifyNow Aspirin Test on patients with acquired non-drug induced platelet abnormalities is not known.
13. Patients who have been treated with Glycoprotein IIb/IIIa inhibitor drugs should not be tested until platelet function has recovered. This time period is approximately 14 days after discontinuation of drug administration for abciximab (ReoPro) and up to 48 hours for eptifibatide (Integrilin) and tirofiban (Aggrastat). The platelet function recovery time varies among individuals and is longer for patients with renal dysfunction.
14. The VerifyNow Aspirin Test results should be interpreted in conjunction with other clinical and laboratory data available to the clinician.

Diagnostic Error Display Messages:

Under certain conditions, a test run may be aborted. In this case, the instrument will display an Error or Attention message. Please refer to the VerifyNow User Manual for a more detailed explanation of these messages.

Maintenance

1. The Maintenance and Setup Icon is used to setup users, change the date and time, recall QC results, network the instrument, set patient ID requirements and for troubleshooting. This function should only be performed by users with proper training and authority. Refer to the User Manual for additional information.
2. Keep the surface of the instrument clean with any commonly used laboratory disinfectant specified in the User Manual. Accumetrics recommends that the exterior surface be cleaned no less than monthly.
3. Cleaning Device: Once every other week, or if the EQC Device fails twice. REMOVE THE TAPE FROM THE CLEANING DEVICE AS INDICATED. Place the device in the test well for 5 seconds and remove. Dispose of the single use cleaning device. Rerun the electronic QC device. If the EQC does not pass, call Accumetrics *Technical Support at 1-800-643-1640.*
4. If the EQC device becomes contaminated, wipe with a damp cloth.
5. Replace the fan filter yearly (see Section 10.2 of the User Manual for additional information).
6. Other than fuse replacement, the external power cord, or parts discussed above no other user-serviceable parts exist on the Verify*Now* Instrument. Contact Accumetrics *Customer Support at 1-800-643-1640* if further service is required.

References:

1. VerifyNow Assay WQC, Package Insert, P/N 14349
2. VerifyNow Aspirin Test, Package Insert, P/N 14314
3. VerifyNow System User Manual, P/N 14340