Impella Right Percutaneous (RP) System: H140001

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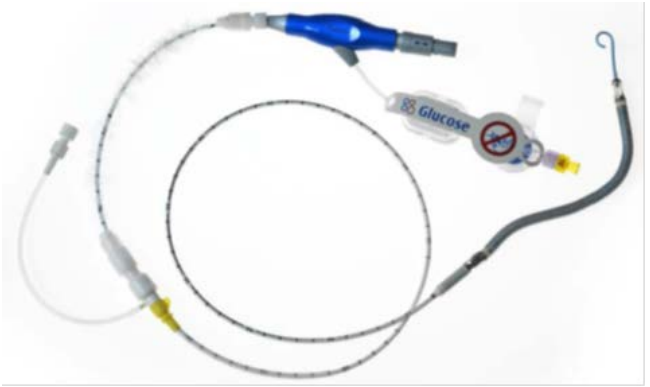
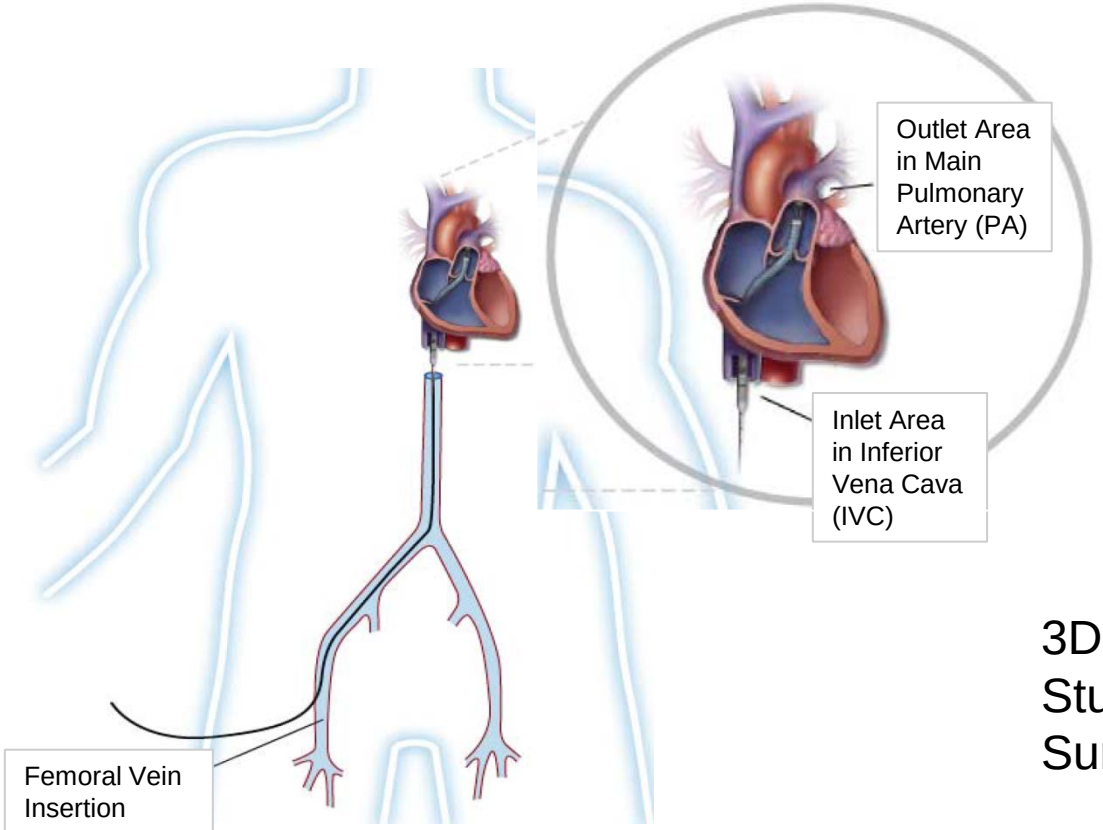
Device Description

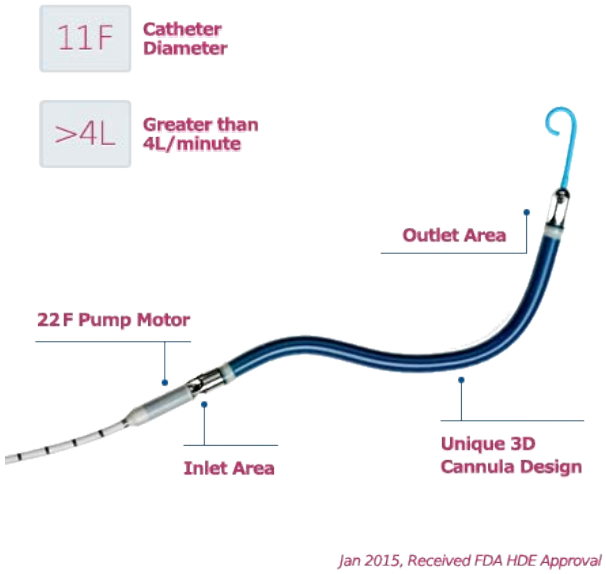
- The Impella RP System is a minimally invasive, miniaturized percutaneous circulatory support system for the right ventricle.
- The main components are a 22 French (F) micro-axial flow pump catheter and The Impella Automated Control Unit
- Designed to provide > 4 Liters (L) of Flow/min



IMPELLA RP Axial Flow Pump

Rapidly Deployable Right-Sided Percutaneous Support





3D CT Human Anatomic Fitting Studies – Appropriate for Body Surface Area (BSA) $\geq 1.5m^{2*}$

*verified by human use

Indication for Use

The Impella RP System is indicated for providing circulatory assistance for up to 14 days in pediatric or adult patients with a body surface area ≥1.5 m^2 who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

Likely Population Examples*:

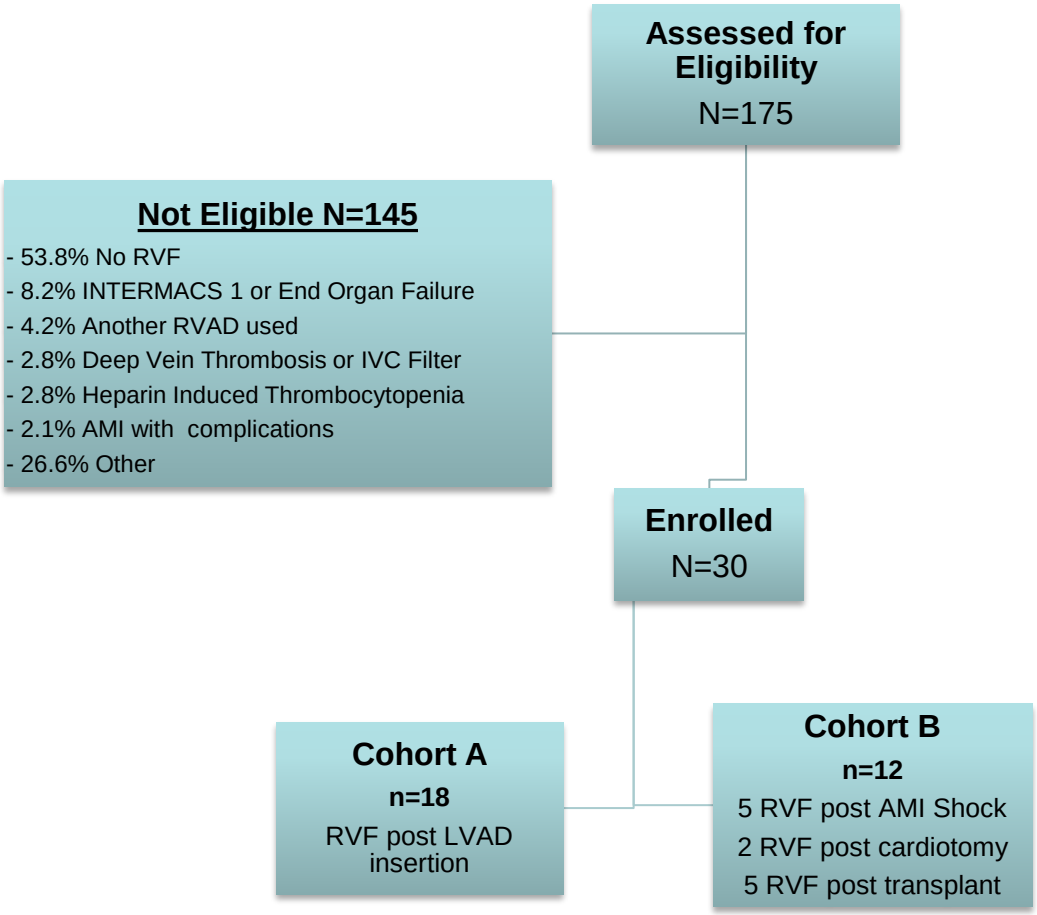
- Patients implanted with a long-term left ventricular assist device (LVAD) for either bridge-to-transplant) or destination therapy who require emergent right ventricular assist device (RVAD).
- Patients who developed right ventricular failure (RVF) as a result of acute myocardial infarction (AMI).
- Heart transplant patients with RVF who require emergent RVAD following transplantation.
- Patients with RVF due to post-cardiotomy cardiogenic shock

*Examples in red = likely plausible pediatric populations

Annual Distribution Number (ADN)

- The humanitarian use designation (HUD) was approved with an ADN = 4,000
- Number of Impella devices sold in the US in 2015: 292
- Number of devices implanted in the US in 2015: 143 implants (0 in pediatric patients)

RECOVER RIGHT TRIAL
A non-randomized safety study



All 30 enrolled patients were treated with the Impella RP and were followed to 30 days post pump removal or hospital discharge, whichever was longer.

Pre-Procedural Characteristics

Major Patient Characteristics*

- Mean age 59.2
  - Range: 24 -86 years
- Male 77%
- 40% African American
- Mean BSA 1.94 $\pm$ 0.22m^2
  - Range 1.5-2.56m^2
- 93% NYHA Class III or IV
- Prior History
  - Coronary artery Disease – 67%
  - Congenital Heart Disease – 12.5%
  - Congestive Heart Failure – 88.5%
  - Diabetes 53%
  - Stroke/Transient Ischemic Attack 16.7%

Major Hemodynamic Characteristics*

- Number of Inotropes 3.2/patient
- Mean Cardiac Index 1.8 $\pm$ 0.2 l/min/m^2
- Pulmonary Capillary Wedge Pressure 17.5 $\pm$ 7.3 mmHg
- Right Atrial Pressure 19.3 $\pm$ 3.9 mmHg
- Mean Arterial Pressure 70.5 $\pm$ 14.3 mmHg
- Heart Rate 90.2 $\pm$ 20.5 beats per minute

* *No significant differences between Cohorts A and B unrelated to Cohort assignment*

Procedural Characteristics Safety and Probable Benefit

Procedural Characteristics:

Procedural Characteristic	All Patients (N=30)	Cohort A (N=18)	Cohort B (N=12)	P-value
Side of Implantation				
Left Femoral Vein	3.3% (1/30)	0.0% (0/18)	8.3% (1/12)	0.213
Right Femoral Vein	96.7% (29/30)	100.0% (18/18)	91.7% (11/12)	0.213
Estimated Blood Loss during Introducer Insertion				
<25mL	89.3% (25/28)	93.8% (15/16)	83.3% (10/12)	0.378
25-50 mL	3.6% (1/28)	0.0% (0/16)	8.3% (1/12)	0.240
>100 mL	7.1% (2/28)	6.3% (1/16)	8.3% (1/12)	0.832
Estimated Blood Loss during RP Placement				
<25mL	60.7% (17/28)	68.8% (11/16)	50.0% (6/12)	0.315
25-50 mL	32.1% (9/28)	25.0% (4/16)	41.7% (5/12)	0.350
>100 mL	7.1% (2/28)	6.3% (1/16)	8.3% (1/12)	0.832
Duration of Support (hours)				
Mean±SD (N)	73.15±37.04 (27)	76.73±31.64 (15)	68.66±43.92 (12)	0.584
Average device flow (L/min)				
Mean±SD (N)	3.23±0.35 (27)	3.14±0.39 (16)	3.35±0.26 (11)	0.143

Primary Endpoint:
Survival at 30 days or discharge post device removal (whichever is longer), or to induction of anesthesia to the next therapy

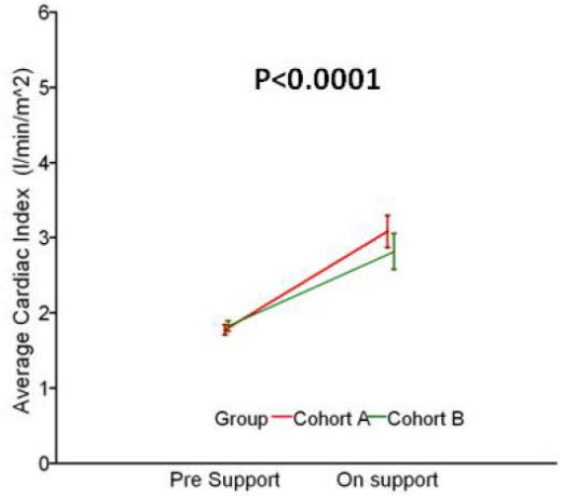
Event	All Patients	Cohort A (N=18)	Cohort B (N=12)
Alive @ 30 days % (n)	73 % (22/30)	83.3% (15/18)	58.3% (7/12)
Alive @ Discharge % (n)	70 % (21/30)	77.8% (14/18)	58.3% (7/12)
Alive at 30day/DC/next therapy %(n)	73 % (22/30)	83.3% (15/18)	58.3% (7/12)

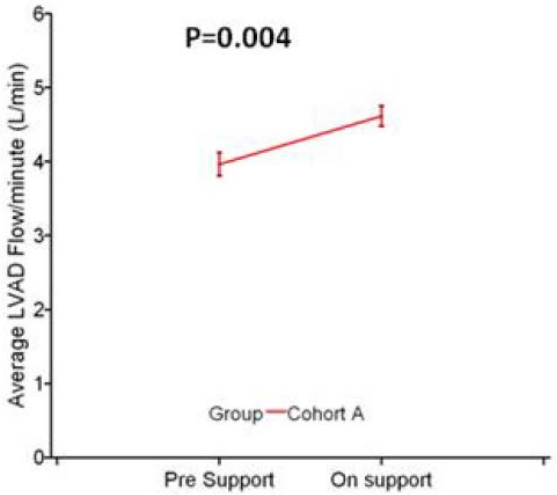
Additional Safety Endpoints:

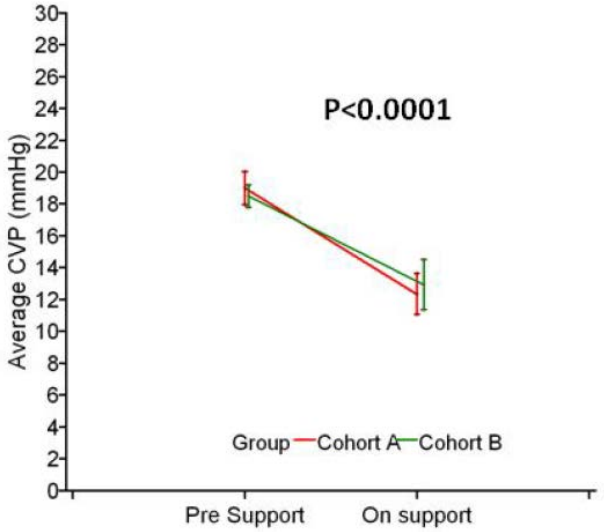
Safety Endpoints	All Patients (N=30)	Cohort A (N=18)	Cohort B (N=12)	P-value
Death	26.7% (8/30)	16.7% (3/18)	41.7% (5/12)	0.129
Major Bleeding	60.0% (18/30)	55.6% (10/18)	66.7% (8/12)	0.543
Hemolysis	13.3% (4/30)	16.7% (3/18)	8.3% (1/12)	0.511
Pulmonary Embolism	0.0% (0/30)	0.0% (0/18)	0.0% (0/12)	--
Tricuspid & Pulmonary Valve Dysfunction*	3.3% (1/30)	5.6% (1/18)	0.0% (0/12)	0.406

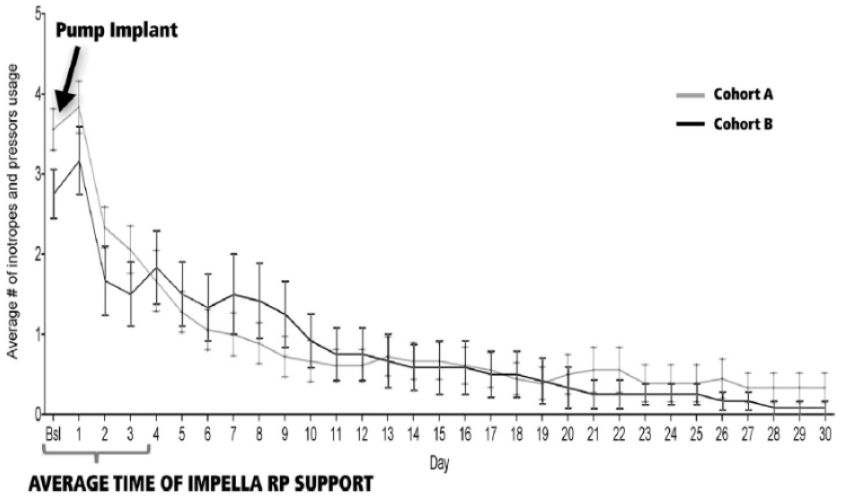
** based on echocardiographic core lab analysis*

Hemodynamic Outcomes



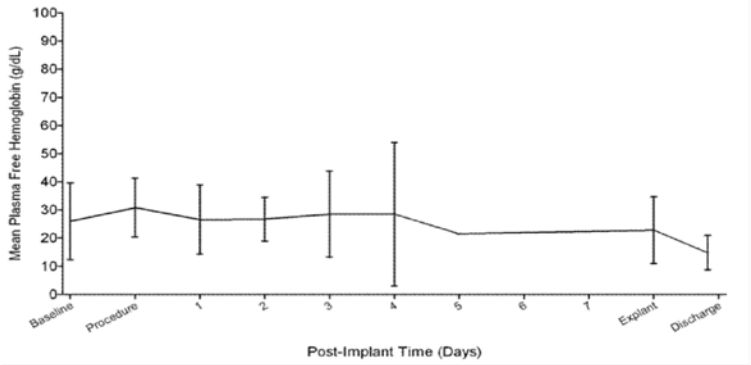




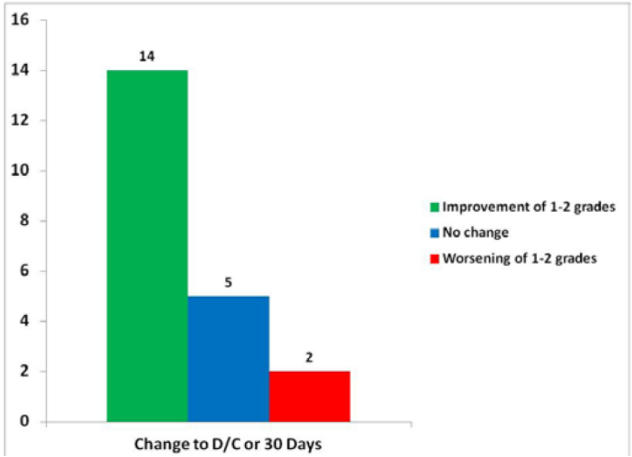


Hemolysis, Right Ventricular (RV) Function and Survival

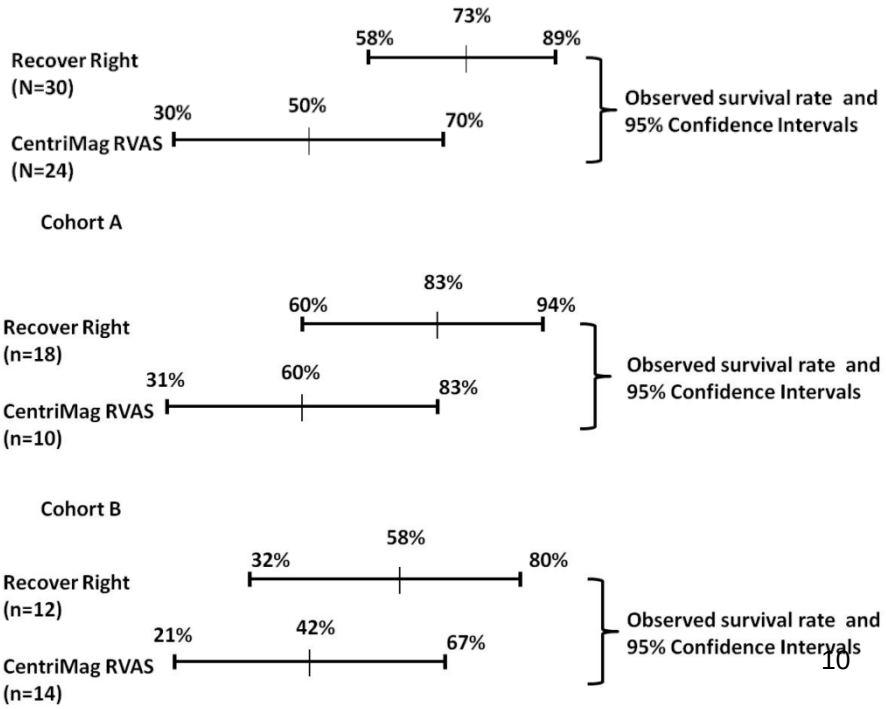
Figure 3.4.11: Plasma Free Hemoglobin temporal trends (patients 007-005 and 013-005 were excluded)



Right ventricular function changes from baseline to 30 day or discharge



Historical Comparison:
Impella RP (Recover Right) vs.
CentriMag RV Assist System (RVAS)



Pediatric Extrapolation

Table 3- Calculated BSA versus age for pediatric patients

Low Range (1.6<BSA≤1.8)		Mid Range (1.8<BSA≤2.0)	
Age (years)	BSA	Age (years)	BSA
15	1.57	19	1.86
16	1.64	20	1.93
17	1.71	21	2.00
18	1.79		

Table 4- Safety endpoint outcomes analysis from the RECOVER RIGHT trial.

Safety Endpoints	Patients having BSAs similar to the pediatric cohorts (15-21 years old) (N=16)	All Patients (N=30)
Death	25.0% (4/16)	26.7% (8/30)
Major Bleeding	68.7% (11/16)	60.0% (18/30)
Hemolysis	18.8% (3/16)	13.3% (4/30)
Pulmonary Embolism	0.0% (0/16)	0.0% (0/30)
Tricuspid and Pulmonary Valve Dysfunction*	6.3% (1/16)	3.3% (1/30)

Table 2- Safety endpoint outcomes for each BSA tercile (for the 2 pertinent pediatric indications)
(Pediatric Indications = Post Transplant and Post LVAD BTT)

Safety Endpoints	Low Range 1.6<BSA≤1.9 (N=7)	Mid Range 1.9< BSA≤2.1 (N=9)	Upper Range BSA>2.1 (N=9)
Death	28.6% (2/7)	22.2% (2/9)	0.0% (0/9)
Major Bleeding	71.4% (5/7)	66.7% (6/9)	44.4% (4/9)
Hemolysis	14.3% (1/7)	22.2% (2/9)	11.1% (1/9)
Pulmonary Embolism	0.0% (0/7)	0.0% (0/9)	0.0% (0/9)
Tricuspid and Pulmonary Valve Dysfunction*	14.3% (1/7)	0.0% (0/9)	0.0% (0/9)

Regulatory History

- Humanitarian Use Device (HUD) designation: July 13, 2012
- Investigational Device Exemption (IDE) approval: November 8, 2012
- Humanitarian Device Exemption (HDE) approval: January 23, 2015

Impella RP Post Approval Studies (PAS)

Two (2) PAS are required to monitor the safety and probable benefit

- **PAS 1**: Impella RP Prospective Study

  - prospective, single arm, multicenter study

  - patients with acute right ventricular failure or decompensation after left ventricular assist device implantation, post myocardial infarction, post heart transplant or open heart surgery with body surface area ≥ 1.5m^2

Impella RP PAS1 (cont'd)

- **PAS 1**: Impella RP Prospective Study
  - Sample size: 30 patients at 15 sites in the US
  - Follow-up: 30 and 180 days post explant
  - Enrollment status: 13 patients currently enrolled (Age: range 46-81yrs, mean 63yrs)

Impella RP PAS2

- **PAS 2**: Impella RP Pediatric Study
  - Retrospective, single arm, multicenter
  - Pediatric patients < 18 yrs, body surface area ≥ 1.5m^2 that develop right ventricular failure after left ventricular assist device implantation, post myocardial infarction, heart transplant or heart surgery supported with the Impella RP

Impella RP PAS2 (cont'd)

- **PAS 2:** Impella RP Pediatric Study

  - Sample size: up to 15 pediatric patients or all pediatric patients supported with Impella RP at a minimum of 5 sites over 5 yrs (whichever comes first)

  - Enrollment: 2 pediatric sites have been trained and received IRB approval for HUD use of the device as of 1/15/16

  - No patient has been enrolled

Literature Results

- **Literature Search** – Date 1/23/2015- 11/30/2015
  - No published studies on the Impella RP other than a publication on the data submitted to FDA for the HDE approval (the RECOVER RIGHT Study)

Impella RP
Medical Device Report (MDR) Review

MDR Search Criteria:

- Brand Name: Impella RP
- Date Report Entered: January 23, 2015 – November 30, 2015

Search Results: 2 MDRs

- **There were NO pediatric patients**
  - Type of Event: 1 death and 1 serious injury
  - Patient Age and Gender: 2 males both 54 years of age
  - Reporting Country: US

FDA Recommendations and Question to the PAC

FDA recommends continued surveillance and will report the following to the PAC in 2017:

- Annual distribution number
- PAS follow-up results
- Literature review
- MDR review

Question: Does the Committee agree with FDA's conclusions and recommendations?