

FDA Executive Summary

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FDA's Pediatric Advisory Committee

H140001
Impella RP System

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act this review provides a safety update based on the postmarket experience with the use of the Impella RP System. The Impella RP System includes a mini heart pump mounted at the end of a catheter, a console that drives the pump, and an infusion pump that flushes the pump. The heart pump can be implanted in the right side of the heart without open chest surgery to help pump blood in patients who need short-term support. The Impella RP is implanted into the right side of a patient's heart through a small incision in the femoral vein. It helps pump blood from the inferior vena cava, through the heart into the pulmonary artery.

The purpose of this review is to provide the Pediatric Advisory Committee with postmarket safety data, so the committee can advise the Food and Drug Administration (FDA) on potential safety concerns associated with the use of this device in children. This executive summary will include postmarket follow-up of the premarket clinical study, the peer-reviewed literature associated with the device, and postmarket medical device reporting (MDR) for adverse events.

Note that the firm has also received the marketing approval/clearance for the following devices that are not the subject of this review: Impella 2.5 System, Impella 5.0 System, Impella LD System, and Impella CP System.

II. INDICATIONS 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 (BSA) $\geq 1.5 \text{ m}^2$ who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

III. DISCUSSION ON PEDIATRIC USE

The inclusion criteria for the pivotal trial included a sub-set of older pediatric patients (from 18 to 21 years old). However, during the trial, there were no patients in this age group enrolled and the youngest patient in the trial was 25 years old. It is expected that a subset of older pediatric patients exists who will be treated with the device, because a sizeable number of pediatric patients receive heart transplants and a significant proportion of these patients are implanted with bridge-to-transplant (BTT) left ventricular assist devices (LVADs) prior to transplant. Based on the computed tomography (CT) fitting study for the Impella RP cannula design completed over a range of BSAs, it is believed that a minimum BSA of $\sim 1.5 \text{ m}^2$ would be compatible for the Impella RP cannula, which corresponds to the average BSA of a 15 year old.

IV. DEVICE DESCRIPTION

The Impella RP System is a minimally invasive, miniaturized percutaneous circulatory support system for the right ventricle. It is comprised of three components: the Impella RP Catheter, the AIC controller, and the Impella Purge Cassette. Both the AIC and the Impella

Purge Cassette were 510(k) cleared for use with the Impella family of left heart circulatory support catheters.

During use, the Impella RP Catheter is percutaneously placed across the tricuspid and pulmonic valves via a single femoral venous access. It actively unloads the right ventricle by pumping blood from the inferior vena cava (IVC) into the pulmonary artery (PA). The catheter is connected to the AIC. The AIC generates the signals required to power the drive motor of the catheter and provides the user interface. The AIC also incorporates the disposable Impella Purge Cassette purge system, which provides a pressure barrier to prevent blood from entering the catheter's drive motor. A dextrose (5-40% with 50 Units/ml of heparin added) solution is used as a purge fluid.

V. REGULATORY HISTORY

The device was granted Humanitarian Use Device (HUD) designation on July 13, 2012 by FDA's Office of Orphan Products Development. ABIOMED, Inc. conducted a clinical study (RECOVER RIGHT) of the device in support of their HDE application, and submitted results to FDA in September 2014. The application was approved on January 23, 2015.

VI. ANNUAL DISTRIBUTION NUMBER AND ANNUAL SALES NUMBERS

Section 520(m)(6)(A)(ii) of The Food, Drug, and Cosmetic Act (FD&C) allows HDEs indicated for pediatric use to be sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). On December 13, 2016, the 21st Century Cures Act (Pub. L. No. 114-255) updated the definition of ADN to be the number of devices "reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the United States." Based on this definition, FDA calculates the ADN to be 8,000 multiplied by the number of devices reasonably necessary to treat an individual.

Table 1: Number of devices sold

Calendar Year (Jan - Dec)	Total Sales	Total Implants	Total Pediatric Implants
2015	292	143	0
2016 (through 11/30)	339	288	2

VII. POST-APPROVAL STUDIES (PAS)

As a condition of approval, the sponsor is required to conduct two PAS to monitor the safety and probable benefit of the Impella RP device.

A. STUDY DESIGNS

PAS1: Impella RP Prospective Study

This is a prospective, multicenter, single arm study enrolling new patients with right

ventricular failure (RVF) in need of hemodynamic support. Patients will be followed at 30 and 180 days post device explant.

Study population and sample size

The patient population will consist of patients with RVF in need of hemodynamic support that meet all of the following inclusion criteria:

- Patients that develop acute RVF or decompensation after LVAD implantation, post myocardial infarction, post heart transplant or post open heart surgery,
- Signed informed consent, and
- $BSA \geq 1.5m^2$,

and none of the exclusion criteria below:

- Disorders of the pulmonary artery wall that would preclude placement or correct positioning of the Impella RP device
- Mechanical valves, severe valvular stenosis or valvular regurgitation of the tricuspid or pulmonary valve
- Mural thrombus of the right atrium or vena cava
- Anatomic conditions precluding insertion of the pump
- Other illnesses or therapy requirements precluding use of the pump such as patients not able to be on anticoagulation therapy.
- Presence of a vena cava filter or caval interruption device, unless there is clear access from the femoral vein to the right atrium that is large enough to accommodate a 22 Fr catheter

Patients with RVF will be supported with the Impella RP until recovery, transplantation or implantation with a long-term device.

The patient population in PAS1 will be similar to the RECOVER RIGHT study population. The RECOVER RIGHT study was a prospective, multicenter, non-randomized IDE study that investigated the safety and probable benefit of the Impella RP in 30 patients with right heart failure refractory to medical treatment and in need of hemodynamic support. The study population consisted of two cohorts: Cohort A - patients that developed RVF following LAD implantation (n=18), and Cohort B - patients that developed RVF post-cardiotomy or post myocardial infarction (n=12).

For this post approval study thirty (30) patients will be consecutively enrolled over 24 months at a maximum of 15 sites in the United States, a sample similar to the RECOVER RIGHT study.

Primary endpoints

The primary endpoint is the survival rate at 30 days post device explant or hospital discharge (whichever is longer), or to induction of anesthesia for a longer term therapy, which includes a heart transplant or an implant of a surgical RVAD.

Secondary Safety endpoints

- The rates of the following serious adverse events (SAEs) measured at hospital discharge or to induction of anesthesia for a longer term therapy (including a heart transplant or an implant of a surgical RVAD):
 - Death (any cause of death and cardiac death)
 - Major bleeding
 - Hemolysis
 - Pulmonary embolism

- Survival will be assessed at 180 days post device explant as well.

Other adverse events

- Device failures and malfunctions
- Unanticipated adverse device effects (UADEs)

Secondary Probable Benefit

The secondary probable benefit endpoint is improvement in the following hemodynamic parameters assessed after initiation of Impella RP support:

- Cardiac index
- Central venous pressure
- LVAD flow

Statistical plan

Patients who develop RVF post LVAD implantation in PAS1 will be compared to Cohort A patients of the RECOVER RIGHT study, and patients who develop RVF post myocardial infarction or post-cardiotomy in PAS1 will be compared to Cohort B patients of the RECOVER RIGHT study. The combined patients that match Cohort A and Cohort B will be compared with the overall patient population in the RECOVER RIGHT study. A direct statistical comparison will not be performed due to the limited sample size and lack of statistical power.

PAS2: Impella RP Pediatric Retrospective Study

This is a single-arm, multicenter, retrospective study of pediatric patients 15 to 17 years of age that developed RVF and were supported with the Impella RP device. Patients will be followed at 30 and 180 days post device explant.

Study population and sample size

The study population will comprise of pediatric patients that 1) develop RVF post LVAD implantation, post myocardial infarction, post heart transplant or open heart surgery and 2) age 15-17 years with $BSA \geq 1.5m^2$) meeting none of exclusion criteria.

Fifteen (15) consecutive pediatric patients or all pediatric patients supported with the Impella RP over a 5 year time period (whichever comes first) will be enrolled at a minimum of 5 participating clinical centers.

The Primary and Secondary endpoints and the rest of study elements are the same as for PAS1 and are described above.

B. STUDY STATUS, RESULTS AND ASSEMENTS

The Prospective Post-Approval Study- PAS1-includes one patient age 21 years within the CDRH pediatric age range. One (1) pediatric patient age 16 years, within the pediatric age criteria (15-17 years), has been enrolled in the Pediatric Retrospective Study -PAS2.

PAS1: Impella RP prospective Study

Enrollment status

This section presents a summary of the 24-month PAS report. The database closing date for this report is January 20, 2017. Twelve (12) sites are currently enrolled and eight (8) sites have enrolled patients. A total of 173 patients have been screened to date and 26 patients have been enrolled. One hundred and forty-seven (147) patients failed screening. The main reason for screening failure was absence of RVF. No patient has been lost to follow-up. A brief summary of the enrollment status is shown below (Table 2):

Table 2: Status of PAS1

	Enrollment Target (per Protocol)	Current Enrollment	Percentage (%)
Number of IRB Approvals	15	12	80.0
Number of study sites enrolled	15	12	80.0
Number of patients enrolled	30	26	86.7
Follow-up rate 180 days post Explant (n=13)		13	52 (13/25)*

*Denominator includes all enrolled patients except 1 patient alive at 30 days but not yet 180 days post explant

Demographic information for the 26 patients enrolled is summarized below:

- The ages ranged from 21 to 81 years (mean: 60 ± 15 years).
- Males constituted 58% (15/26) of enrolled patients
- The race distribution is 50% (13) White, 42% (11) Black/African American, 4% (1) Asian and 4% (1) Other

Results

The reasons for Impella RP implantation in enrolled patients are summarized below (Table 3):

Table 3: Reasons for Device Implantation per Approved Indications for Use

Indication	n/N	Percentage (%)
RVF post LVAD Implantation (Cohort A in the Protocol)	11/26	42.0
Acute RVF (after open heart surgery or post-myocardial infarction) (Cohort B in the Protocol)	15/26	58.0

The proportion of patients enrolled following LVAD implantation is 42% (11/26). The proportion of patients enrolled after open heart surgery or MI is 58% (15/26).

The outcomes data for the enrolled patients are summarized in Table 4 below.

Table 4: Treatment Outcomes for Enrolled patients (N=26)

Outcome	Count (n)
Successfully Supported, Discharged, Alive at 30 days	17
Successfully Supported, Discharged, Alive at 180 days	13
Died prior to 180 days	3
Not yet 180 days	1
Transitioned to next therapy*	1
Died in hospital or prior to 30 days	9
Total deaths	12

*This patient died in hospital after transition to next therapy and is counted within the 9 deaths that occurred in hospital or prior to 30days.

Seventeen (17) patients were successfully supported, discharged and alive at 30 days. One (1) additional patient was transitioned to next therapy (died after the transition). Thus 18 patients met the primary endpoint (survival and transition to next therapy). Of the 17 patients alive at 30 days, thirteen (13) were alive at 180 days post explant, three (3) patients died prior to 180 days and one (1) patients is alive but not yet at 180 days post explant. Nine (9) patients died in hospital or prior to 30 days including five (5) weaned patients, three (3) patients on support, and one (1) patient who died after transition to next therapy. In total twelve (12) patients have died in the study.

The clinical event committee (CEC) has adjudicated the death events for all twelve (12) patients who died. The CEC adjudication concluded that one death was probably related to the device and procedure. This patient was a 72 year old female who was admitted with shortness of breath, severe left and right ventricular failure and ejection fraction of 10%.

Also, prior to LVAD placement the patient developed acute kidney failure and left pleural effusion. LVAD placement was performed and Impella RP was placed at the same time for severe RVF. Post procedure the patient continued to require multiple transfusions due to coagulopathy. The patient also developed compartment syndrome of right leg after Impella RP placement which required fasciotomy. The device was removed on Day 6 of placement. It was considered that the right ventricle recovered at that time and no additional mechanical support was needed. However, the patient developed liver, and respiratory failure. Support including IV medication, continuous venovenous hemofiltration (CVVH) and heartmate II were stopped and the patient died 2 days after Impella RP was explanted. The immediate cause of death was sepsis due to cardiogenic shock. Autopsy was declined. The death was adjudicated by the CEC as probably related to device and procedure.

Major bleeding events were reported in eleven (11) patients (42%, 11/26). The CEC adjudicated one (1) major bleeding event as definitely related to the device and procedure. Hemolysis was reported in nine (9) patients (35%, 9/26) and the CEC adjudicated two (2) of the events as definitely related to the device and procedure. There were no events (0 events) of pulmonary embolism reported.

Unanticipated Adverse Events

There were no unanticipated adverse events reported from enrolling sites.

Assessment of PAS1 Study Results

The current enrollment represents approximately 87% (26/30) of the required sample size. The study enrollment has progressed as expected.

The proportion of patients currently enrolled in the PAS that meet the definition of cohort A or B is slightly different when compared with the RECOVER RIGHT Study population. For example, the proportion of patients enrolled with an implantable LVAD (Cohort A in PAS1) (42.% (11/26)), is lower than the proportion of Cohort A patients in the RECOVER RIGHT study (60% (18/30)).

The primary endpoint of survival at 30 days post device explant or hospital discharge (whichever is longer) or support to next therapy is 69.2% (18/26). The survival rate at 30 days in this report is comparable to the rate presented in the 2016 PAC Executive Summary report (66.7%, 8/12). Although the 69.2% success rate is numerically lower than the 73% (22/30) survival rate observed in the RECOVER RIGHT study, the primary endpoint can only be accurately assessed when all subjects are enrolled and have passed 30 days post explant.

The study sites have not reported any unanticipated adverse event. Of the twelve (12) death events adjudicated by the CEC, one (1) death was determined as probably related to the device and procedure. In addition, the CEC adjudicated one (1) of eleven (11) major bleeding events, and two (2) of nine (9) hemolytic events as definitely related to the device and procedure.

Given that the final dataset is not yet available for PAS1 no definite conclusions can be made at this time.

PAS2: Impella RP Pediatric Retrospective Study

Enrollment status and Assessment

As of database closing for this report two (2) pediatric sites have been trained to use the Impella RP. There are currently 127 sites that have IRB approval for HUD use of the Impella RP.

As of this report one (1) pediatric patient has been treated with the Impella RP at one site approved for HUD use. This was a 16 year old male who experienced cardiac arrest at home. The patient was resuscitated in the emergency room after 35 min of CPR, was diagnosed with Arrhythmogenic Right Ventricular Dysplasia (ARVD) and placed on inotropes. An echocardiograph showed significant RVF and depressed left ventricular ejection fraction. A left-sided assist device (Impella CP) was implanted followed by the Impella RP. The patient's hemodynamics were stabilized, urine output increased, and inotropes were reduced. The patient remained on Impella RP support. Weaning was started 4 days after implantation and both devices were successfully explanted 7 days after implantation. The patient was assessed to be neurologically intact, continued to recover in the hospital and was later discharged home.

Assessment

In order to increase enrollment of the pediatric subjects the sponsor plans to train additional pediatric teams on the use of the Impella RP. The sponsor is tracking all HUD sites for potential pediatric cases, and will retrospectively collect the data from all centers who treat pediatric patients with the Impella RP HUD. FDA will continue to monitor pediatric enrollment in this study.

VIII. POSTMARKET LITERATURE REVIEW

A search of the literature was conducted for articles published on Impella from December 1, 2015 to November 30, 2016 using the same search terms as for the previous presentation. Specifically, the following search terms were used: "Right intracardiac microaxial pump" OR "Right ventricular support rotary blood pump" OR "Right intra-cardiac short term assist" OR "RVAD" OR "Impella RP" OR "Impella right percutaneous" OR "Mechanical support AND Impella" OR Percutaneous Right Ventricular Impella" OR "Percutaneous Right Ventricular Assist Device" AND Impella. The search term combinations yielded thirty one (31) articles. There are only two (2) articles specific to Impella RP, one (1) case report¹ and one (1) study based on the data from the RECOVER RIGHT study that was reviewed by the FDA when this device was approved². The remaining articles are not related to the subject device. These articles are related to different devices such as Implella 2.5/5.0, CP or LVAD.

A summary of the case report is presented below:

Morgan JA, O'Neill WW. Percutaneous Right Ventricular Assist Device Support in a Patient Supported by an LVAD. ASAIO J. 2016 Jul-Aug;62(4):e41-2.

This article includes only one adult patient. The patient was a 70 year-old woman with a history of nonischemic dilated cardiomyopathy with an ejection fraction of 10–15%, NYHA class IV, stage D, end-stage heart failure refractory to optimal medical therapy. The patient underwent implantation of a HeartWare ventricular assist device as a destination therapy. The patient’s intraoperative course was complicated by RV failure which was manifested by a significant increase in pressor and inotropic requirements, decreased LVAD flows, hypotension, and malperfusion. The patient received an Impella RP placed percutaneously via the right femoral vein into the pulmonary artery under fluoroscopic and echocardiographic guidance. Post implantation, there was a significant improvement in the patient’s MAP and an increase in LVAD flow, reduction in RV size and improvement in hemodynamics.

There were no device-related complications with the use the Impella RP in the patient. The patient was discharged home on post- operative day 14.

Conclusion of the Literature Review

This case represents successful use of the Impella RP in an elderly patient who required mechanical support while undergoing LVAD implantation. There were no Impella RP related complications reported in this patient. There is currently no data on the use of the Impella RP in pediatric patients in the published literature.

IX. MEDICAL DEVICE REPORTS (MDRS)

A. OVERVIEW OF MDR DATABASE

Each year, the FDA receives several hundred thousand MDRs of suspected device-associated deaths, serious injuries and malfunctions. The MDR database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDR reports can be used effectively to:

- Establish a qualitative snapshot of adverse events for a specific device or device type
- Detect actual or potential device problems used in a “real world” setting/environment, including:
 - rare, serious, or unexpected adverse events;
 - adverse events that occur during long-term device use;
 - adverse events associated with vulnerable populations;
 - off-label use; and
 - use error

B. STRENGTHS AND LIMITATIONS OF MDR DATA

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified and/or additionally biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of device use. Because of this, MDRs comprise only one of the FDA's several important postmarket surveillance data sources. Other limitations of MDRs include:

- MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time, or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.
- Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MDR data is subjected to reporting bias, attributable to potential causes such as reporting practice, increased media attention, and/or other agency regulatory actions.
- MDR data does not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.

C. MDRS ASSOCIATED WITH IMPELLA RP SYSTEM

The Agency received 6 MDRs related to the Abiomed Impella RP System, entered into FDA's MDR database between December 1, 2015 and November 30, 2016. The MDRs were reviewed for factors such as reported device and patient problems, event type, report source, patient age, patient gender, reporting country and the time to event occurrence (TTEO). The TTEO is based on the implant duration where specified in the event text of the MDR or calculated as the time period between the date of implant and date of event. The MDR factors are characterized in the results summary.

Results

Of the 6 MDRs, 5 MDRs were reported by the manufacturer and 1 MDR by a user facility (UF). The reported type of event included 1 death, 4 serious injuries and 1 malfunction. The MDRs were individually reviewed and based on the information, the malfunction report was determined to be an injury report and reclassified, resulting in an adjusted total of 1 death and 5 injuries. The 6 MDRs reported 6 separate patient events.

Patient age and gender were provided in the 5 manufacturer MDRs, but not in the UF report. However, additional follow-up with the firm resulted in identifying the age and gender of this patient. Patient age ranged between 44 and 68 years with the mean age of 59. There were **no pediatric patients** reported in the MDRs. The patient gender included 5 males and 1 female patient.

The reporting country was provided in each MDR and included the United States (US) (5 MDRs) and Denmark (1 MDR).

Reported Problems

The most commonly reported problems in the 6 MDRs were thrombosis/clot formation in the device (2 MDRs (33%)) and device detachment (2 MDRs (33%)). The device detachments involved Impella RP pump breakage into two pieces with fragments retained in the patients. The remaining reported problems included bleeding in 1 MDR (17%) and a device positioning issue in 1 MDR (17%). The reported problems of thrombosis and bleeding identified in this year’s analysis were also reported in the 2016 analysis and are identified as potential adverse events in the instructions for use (IFU). Table 5 below provides the reported problems by type of event in this year’s analysis as compared to the 2016 analysis.

Table 5. Reported Problems by Type of Event in 2017 compared to 2016.

Reported Problem	MDR Count 2017 Analysis (n=6)			MDR Count 2016 Analysis (n=2)		
	Total MDR Count	Death	Injury ¹	Total MDR Count	Death	Injury ¹
Thrombosis/Clot in the Device	2	1	1	1	0	1
Device Detachment	2	0	2	0	0	0
Bleeding	1	0	1	1	1	0
Positioning Issue	1	0	1	0	0	0

¹Serious Injury per regulatory definition (CFR803.3) includes an event that is life-threatening or results in permanent impairment of a body function or permanent damage to a body structure or necessitates medical or surgical intervention(s) to preclude permanent impairment of a body function or permanent damage to a body structure.

The reported problems are further detailed to include specific event, patient information, the TTEO when available, any required intervention and device evaluation results as provided in the MDRs.

Thrombus/Clot in the Device (n=2)

- There was a death of a 56 year old male reported from Denmark in which the patient presented with an ST elevation myocardial infarction (MI) and history of a patent foramen ovale (PFO). The patient was hemodynamically compromised precipitating the implant of the Impella RP. Placement was difficult but within 30 minutes of support, the console alarmed for low purge flow and increased purge pressure. There was no kink in the pump and the purge cassette was exchanged. Alarms continued but the flow issue resolved. Six hours later, the pump stopped running due to high motor current. The patient experienced severe shock with reduced oxygenation and low blood pressure. The Impella RP was restarted and the pump was flowing, but pulsatility was almost absent. The decision was made to change support to extracorporeal membrane oxygenation (ECMO) but the patient expired prior to ECMO placement. The manufacturer investigation determined the cause of Impella RP pump stop was the ingestion of biomaterial

wrapped around the Impeller most likely interfering with purge flow, causing alarms and eventual pump stops. The users did not replace the pump after pump stops and restarting the pump as directed in the IFU. The manufacturer concluded that the ingested biomaterial could have been due to patient's underlying condition of PFO and blood shunting contributing to clot formation.

- A 60 year old female patient was implanted with an Impella RP for decompensated CHF and severe mitral valve regurgitation after MI. The patient had an ejection fraction (EF) of 10-15% and was in cardiogenic shock. The Impella was removed and a clot was found in the device. The UF contacted the firm to assist with troubleshooting and they were unable to resolve the issue. The Impella was removed and the patient received a right ventricular assist device (RVAD).

Device Detachment (n=2)

- There was an injury report of a 68 year old patient with a left ventricular assist device (LVAD) who was supported with the Impella RP for 3 days when the physician attempted to remove the pump. Sutures were removed and the device was pulled back but only the portion up to the inlet cage was removed. Fluoroscopic images revealed the remaining portion of the device was intact in the iliac area. The detached portion was removed with snares and a balloon. There was no further harm to the patient. The cause was determined by the manufacturer to be a high cumulative load imparted to the cannula due to challenging device placement and position during support. This resulted in the deformation of the connection interface between the cannula and pump housing weakening the epoxy bond. The manufacturer provided training to the healthcare providers to manage use of the device during high residual load. FDA has requested additional information from the firm to further clarify details of their investigation of this issue.
- There was an injury report of a very large 63 year old patient with significant adipose tissue. The patient had a history of cardiac disease and was supported with an Impella 5.0 for left ventricular (LV) support after surgery for mitral valve repair. Five days later, the patient was implanted with an Impella RP due to right ventricular (RV) failure. Pump flows were not optimal precipitating the administration of blood products to improve pulsatility and mean arterial pressures (MAP). The patient improved during the night and medications were weaned down. By the end of the 2nd day, pump flows were reduced and the patient was deteriorating prompting the team to explant Impella RP. During device removal, there was resistance and the pump detached with the pump and motor portion lodged in the femoral vein. Because of the patient's risk of coagulopathy to undergo a surgical removal of the Impella RP, the decision was made to wait until the patient's bleeding risk improved. While awaiting improvement, the patient's family decided to withdraw care. The patient expired and the detached portion of the catheter remains in the patient.

Manufacturer analysis of the returned portion of the Impella RP “revealed that the Delo adhesive had filled the etchings of the laser-etched bonding surface, but there was minimal adhesive coverage over the rest of the surface”. The manufacturer determined the cause “was most likely the load created by the steep insertion angle and high manual pressure applied during explant due to the patient’s size”. The firm has initiated a corrective and preventative action plan (CAPA) to address RP cannula detachments. FDA has requested additional information from the firm to further clarify details of their investigation of this issue.

Bleeding (n=1)

- There was an injury report of a 63 year old male with implant of biventricular assist devices (VAD). The patient continued with multiple problems during his hospitalization and multiple stents were placed 11 days after VAD implant. Seven weeks after implant, the LVAD was replaced and one week later the RVAD was removed and replaced with an Impella RP the following day. One day after Impella implant, flows dropped in the Impella RP and LVAD after the patient was turned in bed. The patient began to decompensate, hemoglobin and hematocrit levels dropped and the patient was not oxygenating. A computer tomography (CT) scan revealed a large retroperitoneal bleed of unknown origin. A total of 18 units of blood products were administered. The patient also required two surgical evacuations of the left femoral artery hematoma. The Impella RP was discontinued and removed to place the patient back on ECMO. The device has not been returned to the manufacturer for evaluation; therefore, device analysis could not be performed. The patient’s status and results of the investigation are pending from the firm.

Positioning Issue (n=1)

- There was an injury report of a 44 year old patient on left sided Impella support. The Impella RP was placed for right sided support. The following day, suction alarms occurred thus reducing the performance level which later resolved. On the third day of support with the Impella RP, suction alarms continued and the decision was made to remove and reinsert the same pump for better positioning. There was difficulty in positioning the pump in the proper location; however, the pump was successfully placed. Following placement, the patient exhibited severe hemolysis requiring the administration of 3-5 units of replacement blood products. The Impella RP was removed and a new Impella RP was placed. This pump functioned without issue and the hemolysis resolved. Due to the patient’s medical condition, the family withdrew support 8 days after initial implant and the patient expired. The outcome was reportedly unrelated to the hemolysis event, as the plasma free hemoglobin (Pfhg) levels were elevated prior to implant.

Manufacturer analysis of the pump revealed the ingestion of biomaterial and significant “thrombus around the leading edge of the impeller, as well as the seal

around the purge gap”. It was determined that increased Pfhg levels during support align with suction alarms and improper pump positioning. The manufacturer determined that the hemolysis was caused by possible pump position during suction periods with elevated Pfhg. According to the IFU, performance levels may vary due to suction or incorrect positioning. The IFU addresses suction alarms and troubleshooting steps to mitigate the issue.

The patient events reported in the MDRs do not appear to be reported in the post approval study (PAS) data. The deaths reported in the PAS may not be reflected in the MDRs if the firm does not believe there is evidence to suggest the device caused or contributed to the patient’s death.

Conclusions

There were no pediatric patients reported in the MDRs.

The thrombosis, hemolysis, bleeding and positioning issues reported in the MDRs have been reported in the Investigational Device Exemption (IDE) study, have been identified in the IFU and reflect known complications of this type of device.

FDA has requested additional information from the firm to further clarify details of their investigation into device detachment and bleeding issues.

The PAS data has not been adjudicated to date. The 6 MDR events were not found in the PAS data because of differences in implanting hospitals and date and outcome differences. Therefore, the MDRs and PAS data appears to be mutually exclusive. The deaths reported in the PAS may not be reflected in the MDRs if the firm does not believe there is evidence to suggest the device caused or contributed to the patient’s death.

X. SUMMARY

The FDA did not identify any new safety signals during this review of the Impella RP System HDE annual report, the MDRs received, and the peer-reviewed literature published since the initial approval. As such, the FDA believes that the HDE for this device remains appropriate for the pediatric population for which it was granted. The FDA will continue our routine monitoring of the safety and distribution information for this device.

XI. REFERENCES

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