

# INTERMACS Adverse Event Definitions

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This document contains the following adverse event definitions:

Hemolysis  
Right Heart Failure  
Device Malfunction  
Major Bleeding  
Major Infection  
Neurological Dysfunction  
Renal Dysfunction  
Cardiac Arrhythmias  
Respiratory Failure  
Venous Thromboembolism  
Wound Dehiscence  
Arterial Non-CNS Thromboembolism  
Hepatic Dysfunction  
Hypertension  
Pericardial Fluid Collection  
Myocardial Infarction

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## MCS-ARC Hemolysis Adverse Event

### Minor Hemolysis

A plasma-free hemoglobin value greater than 20 mg/dl or a serum LDH level greater than two and one-half times (2.5 x) the upper limits of the normal range at the implanting center occurring after the first 72 hours post-implant in the absence of clinical symptoms or findings of hemolysis or abnormal pump function (see Major Hemolysis for a list of symptoms and findings) and thought not attributable to laboratory error.

### Major Hemolysis

A plasma-free hemoglobin value greater than 20 mg/dl or a serum LDH level greater than two and one-half times (2.5 x) the upper limits of the normal range at the implanting center occurring after the first 72 hours post-implant and associated with clinical symptoms or findings of hemolysis or abnormal pump function.

Major Hemolysis requires the presence of at least one of the following conditions:

- Hemoglobinuria (“tea-colored urine”)
- Anemia (decrease in hematocrit or hemoglobin level that is out of proportion to levels explainable by chronic illness or usual post- VAD state)
- Hyperbilirubinemia (total bilirubin above 2 mg/dl, with predominately indirect component)
- Pump malfunction and/or abnormal pump parameters as per section on device malfunction

### Note:

- Isolated LDH elevations should not be reported as hemolysis if attributable to laboratory error, hepatic or pulmonary dysfunction. If suspected, confirmatory testing of LDH, LDH isoenzymes and plasma-free hemoglobin within 24 hours should be obtained to rule out laboratory error.
- All causes of hemolysis should be reported regardless of whether they are thought attributable to the device or not.

### The association of the hemolysis event should be classified as:

- **Patient related:** (i.e., hematologic abnormalities)
- **Management related:** (i.e., drug related, secondary pump or IABP related, pump malposition)
- **Device related:** (i.e., related to pump thrombosis or device malfunction)

## MCS-ARC Right Heart Failure Adverse Event

### Early Acute Right Heart Failure

- Need for implantation of a temporary or durable RVAD (including ECMO) concomitant with LVAD implantation (RVAD implanted before the patient leaving the operating room).

### Early post-implant right heart failure

- Need for implantation of a temporary or durable RVAD (including ECMO) within 30 days following LVAD implantation for any duration of time
- Failure to wean from inotropic or vasopressor support or inhaled nitric oxide within 14 days following LVAD implantation or having to initiate this support within 30 days of implant for a duration of at least 14 days.

The primary diagnosis of right heart failure is made by the presence of at least two of the following clinical findings:

- Ascites
- Functionally limiting peripheral edema (> 2+)
- Elevated estimated jugular venous pressure at least halfway up the neck in an upright patient.
- Elevated measured central venous pressure or right atrial pressure ( $\geq 16$  mm Hg)

Or is associated with at least one of the following manifestations:

- Renal failure with serum creatinine > 2 baseline values.
  - Liver injury with an elevation of at least 2 upper limit normal in AST/ALT or total bilirubin > 2.0.
  - SVO<sub>2</sub> < 50%.
  - Cardiac index < 2.2 liter/min/m<sup>2</sup>.
  - Reduction in pump flow of > 30% from the previous baseline in the absence of mechanical causes such as cardiac tamponade or tension pneumothorax.
  - Elevated lactate >3.0 mmol/liter.
- Death occurring in patients within 14 days of LVAD implant who have not received an RVAD but who remain on inotropes or vasopressors at the time of death and meet criteria for the diagnosis of Right Heart Failure on the basis of the above **clinical findings (2 criteria) or manifestations (1 criterion)** will be considered to have early post-implant right heart failure at the time of death. The contribution of early post-implant right heart failure to the death (primary or secondary) will be made by the clinical care team.

**Late RHF**

- Need for implantation of an RVAD (including ECMO) greater than 30 days after an LVAD implantation. This may occur within the index hospitalization for LVAD implant or during subsequent rehospitalization for any diagnosis which resulted in a need for temporary or permanent right-sided mechanical assist devices.
- Hospitalization that occurs greater than 30 days post-implant and which requires intravenous diuretics or inotropic support for at least 72 hours and is associated with:

The diagnosis of right heart failure is made by the presence of at least two of the following clinical findings:

- Ascites
- Functionally limiting peripheral edema (>2+).
- Elevated estimated jugular venous pressure at least halfway up the neck in an upright patient.
- Elevated measured central venous pressure (>16 mm Hg).

Or is associated with at least one of the following manifestations:

- Renal failure with serum creatinine > 2 baseline value
- Liver injury with an elevation of at least 2 upper limit normal in AST/ALT or total bilirubin > 2.0
- A reduction in pump flow of > 30% from the previous baseline in the absence of tamponade
- SVO2 < 50%
- Cardiac index < 2.2 liter/min/m<sup>2</sup>
- Elevated lactate >3.0 mmol/liter

**The association of the RHF event should be classified as:**

- **Patient-related:** (e.g., pre-implant right heart failure, volume overload secondary to non-adherence with medical management, severe aortic regurgitation, cardiorenal syndrome, arrhythmia induced, pulmonary disease, elevated pulmonary vascular resistance).
- **Management-related:** (e.g., related to implant surgery, volume overload, inotropic agent withdrawal).
- **Device-related:** (e.g., associated with Pump malfunction, outflow graft compromise).

## MCS-ARC Device Malfunction Adverse Event

### Device Malfunction

A device malfunction occurs when any component of the MCS system ceases to operate to its designed performance specifications or otherwise fails to perform as intended. Performance specifications include all claims made in the instructions for use. Device malfunctions are further defined as major or minor.

### Major Device Malfunction

Major device malfunction, otherwise known as failure, occurs when one or more of the components of the MCS system either directly causes or could potentially induce a state of inadequate circulatory support (low cardiac output state) or death. A failure that was iatrogenic or recipient-induced will be classified as an Iatrogenic/Recipient- Induced Failure.

A device malfunction or failure is categorized as major when one of the following conditions occurs:

- Death.
- Hospitalization, emergency room visit or prolongation of hospitalization, or escalation of the level of care in an ongoing hospitalization (i.e., transfer to the intensive care unit).
- Life-threatening event (i.e., stroke or TIA, cardiac arrest, heart failure, syncope or near syncopal event, arrhythmia, etc.).
- Results in significant disability or incapacity.
- Requires an intervention to prevent impairment/injury including:
  - Urgent transplantation listing (immediate urgent listing for the transplant).
  - Pump replacement.
  - Pump explant.
  - Pump deactivation without explant or partial explant of components.
  - Breach of integrity of percutaneous lead requiring repair.
  - Operation to repair or replace any internal component of the circulatory support system.
  - Procedure to repair or stent an outflow graft.

**Note:** Replacement or external controller that is done in an inpatient setting for logistical reasons, in an otherwise stable patient, should be considered a minor device malfunction rather than major.

### Minor Device Malfunction

Minor device malfunction includes inadequately functioning external components that require repair or replacement but do not result in 1a to g. Device malfunction does not apply to routine maintenance including replacement of external controller, pneumatic drive unit, electric power supplies, batteries, and interconnecting cables that are not related to a failed component.

## Device Thrombus

Intracorporeal device thrombus represents a special case of major device malfunction and can be categorized as a suspected device thrombus or confirmed device thrombus. Device thrombus will be classified as suspected (see definition below) on the basis of clinical, biochemical, or hemodynamic findings or confirmed (see definition below) on the basis of device inspection or incontrovertible radiologic studies or absence of appropriate Doppler flow signals that confirm thrombus within the device or its conduits that results in or could potentially induce circulatory failure.

## Suspected Device Thrombus

Suspected device thrombus is a device-related malfunction in which clinical or MCSD parameters suggest thrombus on the blood-contacting components of the pump, cannula, or grafts.

**Suspected device thrombosis will be defined as signs and symptoms to include at least 1 of the 3 following criteria:**

- Presence of major hemolysis (including elevation of biochemical markers of hemolysis; i.e., lactate dehydrogenase or plasma-free hemoglobin, or clinical evidence of hemolysis; i.e., hemoglobinuria).
- Presence of heart failure not explained by structural heart disease.
- Abnormal pump parameters consistent with diminished pump output/pump efficiency/pump performance.

### **AND**

**Suspected device thrombus will be accompanied by 1 or more of the following events or interventions:**

- Death
- Stroke or TIA.
- Arterial non-CNS thromboembolism.
- De-novo need for inotrope therapy.
- Treatment with intravenous anti-coagulation (i.e., heparin), intravenous thrombolytics (i.e., tPA), or intravenous anti-platelet therapy (i.e., eptifibatide, tirofiban).
- Pump replacement.
- Pump explantation with or without exchange.
- Pump deactivation without pump removal.
- Operation to repair or replace any internal component of the circulatory support system.
- Urgent transplantation listing (immediate urgent listing for transplant).

## Confirmed device thrombus

Confirmed device thrombus is a major device-related malfunction in which thrombus is confirmed within the blood-contacting surfaces of device inflow cannula or outflow conduit or grafts. This can be reported through direct visual inspection or by incontrovertible contrast radiographic evidence or by the absence of an appropriate Doppler flow signal that results in or could potentially induce circulatory failure or result in thromboembolism.

**Note:**

- Para conduit device thrombus represents a special case of device malfunction whereby thrombus obstructs the outflow graft from the pump. This should be classified as major if the thrombus directly interferes with pump function by obstructing flow and if the pump is replaced because of the thrombus. The event should be classified as minor if there is visible thrombus with the preserved function of the pump but requires surgical intervention (difficult to define minor when it requires surgical intervention). In all instances, visual confirmation of the thrombus is sufficient for confirmation.
- If a suspected device thrombus event is ultimately confirmed through visual inspection following pump replacement, urgent transplantation or on autopsy following death, the event will be maybe reclassified to confirmed device thrombus.

**The association of the device malfunction event should be classified as:**

- **Patient-related:** (i.e., non-adherence with care of device or Instructions for Use, or its peripheral components, non-adherence with the anti-coagulation regimen, pro- coagulation abnormalities)
- **Management-related** (i.e., surgical protocol deviation, sub-optimal anti-coagulation)
- **Device-related:** (i.e., detected in a device at explant or on contrast studies or associated with hemolysis or other controller data consistent with device malfunction.

## MCS-ARC Bleeding Adverse Event

### Type 1

Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional. This type is not relevant during a hospitalization.

### Type 2

Any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for Type 3, 4, or 5 but does meet at least one of the following criteria:

- Requiring non-surgical, medical intervention by a healthcare professional
- Leading to hospitalization or increased level of care
- Prompting evaluation

### Type 3

- **Type 3a**
  - Overt bleeding accompanied by hemoglobin drop of 3 to < 5 g/dl or (1.86–3.1 mmol/liter SI units) (provided hemoglobin drop is related to bleed)  
**OR**
  - Any transfusion with overt bleeding
- **Type 3b**
  - Overt bleeding plus hemoglobin drop 5 g/dl ((3.1 mmol/liter) or greater (provided hemoglobin drop is related to bleed)  
**OR**
  - Cardiac tamponade  
**OR**
  - Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid)  
**OR**
  - Bleeding requiring intravenous vasoactive agents

**Type 4:** VAD implantation-related bleeding (includes concomitant cardiac or non-cardiac surgical procedures)

- Reoperation after the closure of incision or incisions used to implant the VAD to control bleeding
- $\geq 50$  kg:  $\geq 4$ U PRBC within any 48 hours during the first 7 days post-implant.
- $< 50$  kg:  $\geq 20$  cm<sup>3</sup>/kg PRBC within any 24 hours during the first 7 days post-implant.
- Chest tube output  $> 2$  liters within 24 hours.

**Type 5: Fatal bleeding**

- **Type 5a:** Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious
- **Type 5b.** Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation

**The association of the bleeding event should be classified as follows:**

- **Patient-related:** (e.g., coagulopathy unrelated to surgical technique such as non-adherence with anti-coagulation medication resulting in an inappropriately high level of anti-coagulation, hepatic failure)
- **Management-related:** (e.g., related to surgical technique; hypertension; bleeding in the setting of inappropriate levels of anticoagulation) or to mismanagement of anti-coagulants.
- **Pump related:** (e.g., bleeding from the outflow graft, apical connector, or other internal components)

## MCS-ARC Infection Adverse Event

### MCS Related infections

- **Percutaneous lead site infections**
  - **Superficial percutaneous lead infection:** A positive culture from the skin surrounding the percutaneous lead when there is clinical evidence of infection such as pain, fever, drainage, erythema, or leukocytosis coupled with the need to treat with anti-microbial therapy. The percutaneous lead exit site may have drainage and/or the surrounding skin may have erythema. The epithelialization of the percutaneous lead exit site is preserved. The gram stain of the skin specimen at the driveline exit site will contain white blood cells (i.e., positive sign for inflammation).
  - **Deep percutaneous lead infection:** A positive culture from the driveline exit site deep to the epithelium, when there is clinical evidence of infection such as pain, fever, drainage, erythema, or leukocytosis coupled with the need to treat with anti-microbial therapy. The epithelialization of the percutaneous lead exit site is disrupted and no longer preserved or intact, or there is radiographic evidence of findings consistent with infection along the path of the percutaneous lead outside the mediastinum.
- **Infection of external surfaces of an implantable component.** A positive culture from the tissue surrounding the external housing of a pump or one of its components implanted within the body (including device components such as controllers, batteries, etc.), when there is clinical evidence of infection such as pain, fever, drainage, erythema, or leukocytosis coupled with the need to treat with anti-microbial therapy.
- **Infection of blood-contacting surfaces of an implantable component (device endocarditis):** Infection of blood-contacting internal surfaces of the MCS device including inflow/outflow grafts: documented by positive blood cultures or radiographic or echocardiographic evidence of vegetation in blood flow path of the pump coupled with the need to treat with anti-microbial therapy.

### Non-MCS-related infections.

- **Infective Endocarditis:** Non-MCS related Positive blood cultures and echocardiography findings for mass or vegetation only on native valves, ICD, or pacemaker leads.
- **BSI**
  - Positive blood cultures with no other source identified
  - Bloodstream infection: non-VAD site or central venous catheter-related (definition from the Centers for Disease Control/National Healthcare Safety Network)
  - Should be coupled with the need to treat with anti-microbial therapy.
- **Mediastinitis**
  - **Procedure-related mediastinitis**
    - Deep sternal wound infection (isolated)

- Deep sternal wound infection involving MCS device components (continuous with mediastinum or already situated in the mediastinum). Maybe contiguous with implanted components of the MCS device
  - **Non-MCS-related mediastinitis:**
    - Mediastinitis definitively owing to another cause (e.g., esophageal perforation during endoscopy, contiguous with empyema).
  - **Superficial mediastinal or thoracotomy wound infection**
    - Infection involving only skin, sub-cutaneous fat, and muscle of implant incision.
    - Should be coupled with the need to treat with anti-microbial therapy.
- **Sepsis**
  - Life-threatening organ dysfunction caused by a dysregulated host response to infection with:
    - Evidence of systemic involvement by infection, manifested by need to treat with anti-microbial therapy
    - Positive blood cultures and/or two of the following:
      - PaO<sub>2</sub>/FIO<sub>2</sub> < 400 or respiratory rate ≥ 22/min or ventilated respiratory support
      - Hypotension with systolic BP < 100 mm Hg or MAP ≤ 65 mm Hg.
      - Platelet count < 150 or elevated prothrombin time or fibrinogen degradation products
      - Bilirubin (serum) > 50% above baseline
      - Altered mental status (Glasgow score < 15)
      - Creatinine (serum) > 50% above baseline
      - Need for intravenous vasoconstricting agents
- **Localized non-MCS device infection:** Infection localized to a site not involving the MCS device or components (e.g., pneumonia, urinary tract infection, cholecystitis, diverticulitis, dental abscess) coupled with the need to treat with anti-microbial therapy

**The association of the infection event should be classified as:**

- **Patient-related:** (e.g., non-adherence or poor management of driveline exit site or indwelling catheters, IV drug abuse, aspiration)
- **Management-related:** (e.g., improper tunneling, contamination of the intraoperative site, prolonged intubation)
- **Device-related:** (e.g., Device endocarditis diagnosed by radiological examination or detection of pannus within the conduits or device)

## MCS-ARC Neurologic Dysfunction Adverse Event

**Type 1:** Overt CNS injury: acutely symptomatic brain or spinal cord injury

- **Type 1a - Ischemic stroke:** Sudden onset of neurologic signs or symptoms fitting a focal or multifocal vascular territory within the brain, spinal cord, or retina, that:
  - Persist for  $\geq$  24 hours or until death, with pathology or neuroimaging evidence that demonstrates either:
    - CNS infarction in the corresponding vascular territory (with or without hemorrhage); or
    - Absence of other apparent causes (including hemorrhage), even if no evidence of acute ischemia in the corresponding vascular territory is detected.

### OR

- Symptoms lasting < 24 hours with pathology or neuroimaging confirmation of CNS infarction in the corresponding vascular territory. Note: when CNS infarction location does not match the transient symptoms, the event would be classified as covert CNS infarction (Type 2a) and a TIA (Type 3a), but not an ischemic stroke.

**Note:** Signs and symptoms consistent with stroke typically include an acute onset of one of the following: focal weakness and/or numbness, impaired language production or comprehension, homonymous hemianopia or quadrantanopia, diplopia, altitudinal monocular blindness, hemispatial neglect, dysarthria, vertigo, or ataxia.

- **Type 1aH - Ischemic stroke with hemorrhagic conversion:** Ischemic stroke includes hemorrhagic conversions. These should be sub-classified as Class A or B when an ischemic stroke is the primary mechanism and pathology, or neuroimaging confirms a hemorrhagic conversion.
  - **Class A- Petechial (non-space-occupying) hemorrhage:** Petechiae or confluent petechiae within the infarction or its margins, but without a space-occupying effect.
  - **Class B – confluent (space-occupying) hemorrhage:** Confluent hemorrhage or hematoma originating from within the infarcted area with space-occupying effect.
- **Type 1b - Symptomatic intracerebral hemorrhage:** Rapidly developing neurologic signs or symptoms (focal or global) caused by an intraparenchymal, intraventricular, spinal cord, or retinal collection of blood, not caused by trauma.
- **Type 1c - Symptomatic Sub-arachnoid hemorrhage:** Rapidly developing neurologic signs or symptoms (focal or global) and/or headache caused by bleeding into the sub-arachnoid space, not caused by trauma.
- **Type 1d - Stroke, not otherwise specified:** An episode of acute focal neurologic signs or symptoms and/or headache presumed to be caused by CNS ischemia or CNS hemorrhage, persisting 24 hours or until death, but without sufficient evidence to be classified as one of the above (i.e., no neuroimaging performed).

- **Type 1e - Symptomatic hypoxic-ischemic injury:** Non-focal (global) neurologic signs or symptoms due to diffuse brain, spinal cord, or retinal cell death (confirmed by pathology or neuroimaging) in a non-vascular distribution, attributable to hypotension and/or hypoxia.
- **Type 1f - Symptomatic sub-dural hemorrhage:** An episode of acute focal neurologic signs or symptoms and/or headache accompanied by evidence of bleeding into the sub-dural space.
- **Type 1g – Traumatic Brain Injury Intracerebral, Subarachnoid or subdural:** A brain bleed due to an injury. Examples: Falls, Motor Vehicle accident.

**Type 2:** Covert CNS injury: Acutely asymptomatic brain or spinal cord injury detected by neuroimaging

- **Type 2a - Covert CNS infarction:** Brain, spinal cord, or retinal cell death attributable to focal or multifocal ischemia on the basis of neuroimaging or pathologic evidence of CNS infarction, without a history of acute neurologic symptoms consistent with the lesion location.
- **Type 2aH - Covert CNS infarction with hemorrhagic conversion:** Covert CNS infarction includes hemorrhagic conversions. These should be sub-classified as Class A or B when CNS infarction is the primary mechanism and neuroimaging, or pathology confirms a hemorrhagic conversion.
  - **Class A - Petechial (non-space-occupying) hemorrhage:** Petechiae or confluent petechiae within the infarction or its margins, but without a space-occupying effect
  - **Class B - Confluent (space-occupying) hemorrhage:** Confluent hemorrhage originating from within the infarcted area with space-occupying effect
- **Type 2b - Covert CNS hemorrhage:** Neuroimaging or pathologic evidence of CNS hemorrhage within the brain parenchyma, sub-arachnoid space, sub-dural space, ventricular system, spinal cord or retina on neuroimaging that is not caused by trauma, without a history of acute neurologic symptoms consistent with the bleeding location

**Type 3:** Neurologic dysfunction (acutely symptomatic) without CNS injury

- **Type 3a - TIA:** Transient focal neurologic signs or symptoms (lasting < 24 hours) presumed to be owing to the focal brain, spinal cord, or retinal ischemia, but without evidence of acute infarction by neuroimaging or pathology (or in the absence of imaging)
- **Type 3b - Delirium without CNS injury:** Transient non-focal (global) neurologic signs or symptoms (variable duration) without evidence of cell death by neuroimaging or pathology
- **Seizures – (abstraction from places seizures under the sub-types for Type 3)**

**Classification of Acute Severity, Recovery and Long-Term Disability**

- **Acute Severity**
  - **Mild neurologic dysfunction:** NIHSS 0-5
  - **Moderate neurologic dysfunction:** NIHSS 6-14
  - **Severe neurologic dysfunction:** NIHSS  $\geq$ 15

**Note:** Severity assessment should be performed at the time of diagnosis of any overt CNS injury (Types 1) to ensure accurate classification

- **Stroke Recovery**

- **Stroke with complete recovery:** A modified Rankin Score (MRS) at 30-90 days of 0 OR a return to the patient's pre- stroke baseline MRS, in the absence of any ongoing new symptoms due to the stroke.

- **Stroke Disability**

- **Fatal Stroke:** Death resulting from a stroke where the cause of death is attributable to the stroke.
- **Disabling stroke:** An MRS  $\geq 2$  at 30-90 days with an increase of at least 1 point compared to the pre-stroke baseline.
- **Non-disabling stroke:** An MRS  $< 2$  at 30-90 days, or  $\geq 2$  without an increase of at least 1 compared to the pre- stroke baseline.

**Note:** Disability assessment applies only to subjects with overt CNS injury (Type 1) and should be performed at  $90 \pm 14$  days after the stroke event.

**The association of the neurologic event should be classified as:**

- **Patient-related:** (e.g., documentation of previous carotid or cerebrovascular disease, coagulopathy unrelated to surgical technique such as non-adherence with anti-coagulation medication resulting in an inappropriately high level of anti-coagulation, related to illicit drug use, non-adherence with other medications, trauma, associated with sepsis)
- **Management-related:** (e.g., over anti-coagulation or associated with the use of accessory assist device, hypotension or hypertension-related to surgical procedure)
- **Device-related:** (e.g. secondary to pump thrombosis or device malfunction)

## MSC-ARC Renal Dysfunction Adverse Event

### Acute Renal Dysfunction

- **Stage 1**
  - Increase in serum creatinine to 150% to 199% (1.5–1.99 x increase compared with baseline) or increase of > 0.3 mg/dl (> 26.4 mmol/liter) or
  - Urine output < 0.5 ml/kg/h for > 6 but < 12 hours.
- **Stage 2**
  - Increase in serum creatinine to 200% to 299% (2.0 x –2.99 x increase compared with baseline) or
  - Urine output < 0.5 ml/kg/h for > 12 but < 24 hours.
- **Stage 3**
  - Increase in serum creatinine to >300% (>3 x increase compared with baseline) or
  - Serum creatinine of > 4.0 mg/dl (>354 mmol/liter) with an acute increase of at least 0.5 mg/dl (44 mmol/liter) or
  - Urine output <0.3 ml/kg/h for >24 hours or
  - Anuria for >12 hours or
  - Need for renal replacement therapy (includes dialysis or ultrafiltration) regardless of above criteria.

### Chronic Renal Dysfunction

An increase in serum creatinine of 2 mg/dl or greater above baseline, or requirement for renal replacement therapy, either of which is sustained for at least 90 days.

### The association of the renal dysfunction event should be classified as follows:

- **Patient-related:** (e.g., non-adherence to medical therapy resulting in renal dysfunction).
- **Management-related:** (e.g., overprescribing of diuretic therapy or administration of renal toxic drugs or contrast agents that result in renal dysfunction).
- **Device-related:** (e.g., device failure resulting in renal dysfunction).

## MCS-ARC Cardiac Arrhythmias

Any documented arrhythmia that results in clinical compromise (e.g., abnormal VAD function [e.g., diminished VAD flow or suction events], oliguria, pre-syncope or syncope, angina, dyspnea), or requires hospitalization or treatment (drug therapy, defibrillation, cardioversion, ICD therapy (e.g., shock or anti-tachycardia pacing) or arrhythmia ablation procedure).

**Cardiac arrhythmias are classified as 1 of 2 types:**

- **Sustained ventricular arrhythmia** resulting in clinical compromise, or requiring hospitalization or drug treatment, defibrillation, cardioversion, ICD therapy, or arrhythmia ablation procedure.
- **Sustained supraventricular arrhythmia** resulting in clinical compromise, or requiring hospitalization or drug treatment, cardioversion, ICD therapy, or arrhythmia ablation procedure.

**The association of the cardiac arrhythmia event should be classified as:**

- **Patient-related:** (e.g., recurrence of pre-operative arrhythmia non-adherence with medications).
- **Management-related:** (e.g., related to uncorrected electrolyte imbalance, Swan Ganz malposition, secondary to cardiac tamponade).
- **Device-related:** (e.g., Pump malfunction, malposition of pump, or inflow cannula).

## MCS-ARC Respiratory Failure

Impairment of respiratory function requiring reintubation, tracheostomy, or the inability to discontinue ventilatory support within 6 days (144 hours) post-VAD implant. This excludes intubation for reoperation or temporary intubation for diagnostic or therapeutic procedures.

**The association of the respiratory failure event should be classified as follows:**

- **Patient-related:** (e.g., non-adherence to medical therapy resulting in respiratory failure).
- **Management-related:** (e.g., inadequate diuretic therapy resulting in respiratory dysfunction).
- **Device-related:** (e.g., device failure resulting in respiratory dysfunction).

## MCS-ARC Venous Thromboembolism

Evidence of venous thromboembolic event (e.g., deep vein thrombosis, pulmonary embolism) by standard clinical and laboratory testing.

## MCS-ARC Wound Dehiscence

Disruption of the apposed surfaces of a surgical incision, excluding infectious etiology, and requiring surgical repair.

## **MCS-ARC Arterial non-CNS Thromboembolism**

An acute systemic arterial perfusion deficit in any non-cerebrovascular organ system due to thromboembolism [confirmed by 1 or more of the following](#):

- Standard clinical and laboratory testing
- Operative findings
- Autopsy findings

**Note:** This definition excludes neurologic events.

## **MCS-ARC Hepatic Dysfunction**

An increase in any two of the following hepatic laboratory values (total bilirubin, AST, and ALT) to a level greater than 3 times the upper limit of normal for the hospital, beyond 14 days post-implant (or if hepatic dysfunction is the primary cause of death).

## **MCS-ARC Hypertension: Adult**

New-onset blood pressure elevation greater than or equal to 140 mm Hg systolic or 90 mm Hg diastolic (pulsatile pump) or 110 mm Hg mean pressure (rotary pump).

## **MCS-ARC Psychiatric Episode:**

Disturbance in thinking, emotion or behavior that causes substantial impairment in functioning or marked subjective distress and requires intervention. Intervention is the addition of new psychiatric medication, hospitalization, or referral to a mental health professional for treatment. Suicide is included in this definition.

**The psychiatric event should be classified according to the DSM 5 classification:**

- **Axis I:** Clinical disorders, including anxiety disorders, mood disorders, schizophrenia and other psychotic disorders.
- **Axis II:** Personality disorders and mental retardation.
- **Axis III:** General medical conditions.
- **Axis IV:** Psychosocial and environmental problems.

## **MCS-ARC Pericardial Fluid Collection:**

Accumulation of fluid or clot in the pericardial space that requires surgical intervention or percutaneous catheter drainage. This event will be subdivided into those with clinical signs of tamponade (e.g. increased central venous pressure and decreased cardiac/VAD output) and those without signs of tamponade.

## **MCS-ARC Myocardial Infarction:**

Two categories of myocardial infarction will be identified:

- **Peri-Operative Myocardial Infarction:** The clinical suspicion of myocardial infarction together with CK-MB or Troponin > 10 times the local hospital upper limits of normal, found within 7 days following VAD implant together with ECG findings consistent with acute myocardial infarction. (This definition uses the higher suggested limit for serum markers due to apical coring at the time of VAD placement and does not use wall motion changes because the apical sewing ring inherently creates new wall motion abnormalities.)
- **Non-Perioperative Myocardial Infarction:** The presence at > 7 days post-implant of two of the following three criteria:
  - Chest pain which is characteristic of myocardial ischemia,
  - ECG with a pattern or changes consistent with a myocardial infarction, and
  - Troponin or CK (measured by standard clinical pathology/laboratory medicine methods) greater than the normal range for the local hospital with positive MB fraction ( $\geq 3\%$  total CK). This should be accompanied by a new regional LV or RV wall motion abnormality on a myocardial imaging study.