STeroids to REduce Systemic inflammation after infant heart Surgery (STRESS trial)

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1 OVERVIEW

Congenital heart diseases (CHD) are the most common birth defects, occurring in nearly 1% of live births. Every year, an estimated 40,000 infants born in the U.S. suffer from CHD. Despite advances in surgical management, CHD requiring neonatal surgery is associated with poor outcomes; national registry data demonstrates post-operative major morbidity in 23% and 10% do not survive to hospital discharge.[1-4]

Poor outcomes after pediatric heart surgery are often attributable to a severe systemic inflammatory response to cardiopulmonary bypass (CPB).[5-8] CPB is necessary for most infant CHD surgeries. Therefore, to reduce the post-CPB inflammatory reaction, many surgeons administer pre-or intra-operative steroids.[9-15] Steroids have been shown to reduce inflammatory markers after neonatal heart surgery.[13, 16] However, steroids also have potential harmful effects including an increased risk of post-operative infection.[17] The recent SIRS trial evaluated the safety and efficacy of steroids after CPB in adults and demonstrated no beneficial effect of steroids but increased risk of post-CPB myocardial infarction and other major adverse events.[18, 19]

Adult trial results cannot be reliably extrapolated to infants because the neonatal response to CPB is markedly different to that seen in adults; infants demonstrate both a more pronounced inflammatory reaction and a different post-operative complication profile. For these reasons approximately 60% of congenital heart surgeons continue to administer perioperative steroids to infants undergoing heart surgery.[17] Yet this practice is not evidence based as no safety/efficacy trial has ever evaluated steroids in infants undergoing heart surgery with CPB. Several smaller steroid trials (all enrolling < 75 patients) have focused on surrogate outcome measures, but none have provided conclusive data.[16, 20]

The major barrier to performing a steroid trial in infants with CHD has been the high cost associated with trial conduct for these relatively rare defects. To overcome this barrier, we will use a novel approach leveraging existing registry infrastructure at CHD surgical sites that participate in the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD). Sites participating in the STS-CHSD collect data into their institutional databases using standardized case report forms (see Appendix A) so that the data can be exported to the STS-CHSD. These sites already employ data coordinating specialists to capture patient demographics, procedural variables, and post-operative outcomes (including a list of over 60 complication variables) using strict and consistent data element definitions. By leveraging these site-specific resources we project that we can reduce trial costs by >75%.

2 PROTOCOL SYNOPSIS

Protocol Title	**STeroids to REduce Systemic inflammation after infant heart Surgery (STRESS trial)**
US IND Number	129266
Grant number	UO1TR001803-01
Product	Intravenous methylprednisolone
Objectives:	To determine the pharmacokinetics (PK)/pharmacodynamics (PD), safety and efficacy of methylprednisolone in infants undergoing planned heart surgery with cardiopulmonary bypass
Study Design:	This is a prospective, double blind, multi-center, placebo-controlled safety and efficacy study. Blood samples will be collected from a subset of enrolled study participants to evaluate single dose methylprednisolone PK/PD. After informed consent is obtained, participants will be randomized in a 1:1 fashion to intravenous methylprednisolone versus placebo. Study drug/placebo will be administered in the operating room at the time of initiation of cardiopulmonary bypass. Patients will be followed for primary and secondary outcomes for the duration of their hospitalization. Serious study drug-related adverse events will be collected for 7 days after the administration of study drug.
Rationale for study design	The study design will allow for evaluation of safety and efficacy to neonates receiving the drug. The proposed design will also allow for characterization of single dose methylprednisolone PK/PD.
Study Population:	Up to 1500 infants ages < 1 year undergoing planned heart surgery with cardiopulmonary bypass including a minimum of 400 neonates ≤ 30 days at the time of surgery.
Number of Sites:	Up to 40
Duration of Subject Participation:	Until hospital discharge
Dose ranges to be studied	Intravenous methylprednisolone will be administered using a preservative free formulation. The dosage in this study will be 30 mg/kg
Dose Schedule:	Intraoperative methylprednisolone/placebo administered as a single IV dose into the cardiopulmonary bypass pump prime
Diagnosis and Main Criteria for Inclusion	Inclusion criteria: 1. Age < 1 year at the time of surgery 2. Undergoing planned heart surgery with CPB as part of standard clinical care. 3. Availability and willingness of the parent/legally authorized representative to provide written informed consent. Exclusion criteria: 1. < 37 weeks adjusted gestational age at time of surgery

	2. Any oral or intravenous steroid treatment within two days of surgery 3. Infection contraindicating steroid use 4. Any patient receiving any of the following medications within 2 days of surgery: Amphoteracin B, aminoglutethimide, anticholesterases, warfarin, P450 3A4 inducers including (but not limited to) carbamazepine, phenobarbital, phenytoin, rifampin, bosentan and nafcillin or P450 3A4 inhibitors including (but not limited to) clarithromycin, voriconazole, itraconazole, ketoconazole, ciprofloxacin, diltiazem, fluconazole, erythromycin, azithromycin and verapamil. 5. Preoperative mechanical circulatory support or active resuscitation at the time of randomization 6. Previous enrollment in the STRESS trial
Estimated Start:	September 2017
Estimated Finish:	August 2021
Primary endpoints	Primary efficacy and safety outcome measures will be compared between infants receiving any methylprednisolone and placebo. <u>Primary endpoint - efficacy:</u> The primary outcome measure will consist of a composite mortality, major morbidity and length of stay global rank endpoint with endpoints ranked according to severity. For this endpoint each randomized patient recieving study drug will be assigned a rank based upon their most-severe outcome.
Secondary endpoints	<u>Efficacy:</u> • Mortality including in-hospital mortality or mortality after hospital discharge but within 30 days of the last dose of study drug • Death or major complication as defined by an outcome in one of the 6 highest global ranking categories • Post-operative hospital length of stay • Prevalence of prolonged (> 7 days) post-operative mechanical ventilation • Occurrence of post-operative low cardiac output syndrome <u>Safety:</u> • Occurence of any one or more of the following major post-operative infectious complications: o Postprocedural infective endocarditis o Pneumonia o Sepsis o Deep wound infection o Mediastinitis • Other post-operative complications will be collected from the start of study drug administration until hospital discharge. <u>PK/PD/Biomarkers:</u> • Time to maximum concentration (T_{max}) • Maximum concentration (C_{max}) • Clearance (CL) • Volume of distribution (Vd) • Post-operative blood markers of inflammation

PK/PD/Biomarkers:	Blood samples will be obtained from patients at various time points after the study drug infusion. PK parameters will be estimated by non-compartmental analysis using WinNonLin software. Study participants as well as enrolling centers will be given the opportunity to not participate in the PK/PD and/or Biomarker studies as these require needle sticks. Therefore it is expected that PK/PD and/or biomarker data will not be collected on every participant enrolled in the STRESS trial
Criteria for evaluation	Safety/Efficacy: Safety and efficacy data will be collected at participating sites using their existing surgical databases (STS-CHSD). The majority of efficacy and safety outcomes represent data elements that sites are currently collecting for submission to the STS-CHSD. A separate clinical database will be used for expedited reporting of any study drug-related serious adverse events. An independent Data Monitoring Board (DMC) will monitor the conduct of the trial for performance (e.g., recruitment, flow and quality control of data, adherence to the protocol) and patient safety. The DMC may review the data at any time. At any time and for any reason, the DMC may recommend to the sponsor that the trial be interrupted or discontinued. Pharmacokinetics: Methylprednisolone concentrations will be measured in plasma. Samples will be measured at a central lab using a validated bioanalytical assay.
Statistical Consideration:	This protocol has sufficient enrollment to evaluate PK/PD, safety and efficacy of IV methylprednisolone

3 BACKGROUND INFORMATION

3.1 Summary of Experience in the Perioperative Setting in Children with CHD

Some surgeons/centers currently administer perioperative high dose (20mg to 60mg) intravenous methylprednisolone before pediatric heart surgery with CPB. In a national registry study of > 3000 neonates with data capture spanning 2004 to 2008, 62% of neonates undergoing surgery with CPB received perioperative methylprednisolone while 38% did not. Of those receiving methylprednisolone, 22% received methylprednisolone on both the day before, and day of surgery, 12% on the day before surgery only, and 28% on the day of surgery only. In a 2nd national registry study including > 25,000 infants undergoing CPB operations (2003-2008), 57% received perioperative corticosteroids while 43% did not.[21] Results of a survey of surgeons from the Congenital Heart Surgeon's Society were similar; 28% did not routinely use steroids for neonatal heart surgery. Of the 72% that did routinely use steroids, ~1/3rd administered steroids pre-operatively and intra-operatively and the remainder gave intra-operative steroids only.[22]

Several previous small translationally focused clinical trials have evaluated the safety and efficacy of methylprednisolone. In the largest contemporary trial, neonates scheduled for cardiac surgery were prospectively randomized to receive either 2-dose (8 hours preoperatively and operatively, n = 39) or single-dose (operatively, n = 37) methylprednisolone at 30 mg/kg IV per dose in a prospective double-blind trial. Neonates receiving pre-operative methylprednisolone therapy demonstrated significantly reduced pre-operative pro-inflammatory cytokines including interleukin-6 and 8. There were no differences between the two groups in post-operative pro-inflammatory markers and no differences in the incidence of post-operative low cardiac output syndrome. [13, 14] Methylprednisolone was well tolerated with no adverse drug reactions. The overall incidence of post-operative infection was 13% (10/76) and 4% (3/76) received a post-operative insulin infusion for hyperglycemia.

A meta-analysis evaluated six previous steroid trials in children undergoing heart surgery with CPB. The combined enrollment of these six trials was 232 participants including 116 receiving peri-operative steroids; two of these studies used methylprednisolone at doses of 30mg/kg IV per dose (n=67 patients). The results of this meta-analysis demonstrated a nonsignificant trend of reduced mortality in steroid-treated patients (11 [4.7%] vs 4 [1.7%] patients; odds ratio, 0.41; 95% CI, 0.14–1.15; p = 0.089). Steroids had no effects on mechanical ventilation time (117.4 ± 95.9 hr vs 137.3 ± 102.4 hr; p = 0.43) and ICU length of stay (9.6 ± 4.6 d vs 9.9 ± 5.9 d; p = 0.8). Perioperative steroid administration reduced the prevalence of renal dysfunction (13 [54.2%] vs 2 [8%] patients; odds ratio, 0.07; 95% CI, 0.01–0.38; p = 0.002). There were no significant differences in the adverse event profiles for patients receiving steroids versus placebo.[20]

The conclusions of the aforementioned studies, as well as several associated editorials have all been that a large, randomized, controlled trial is needed to evaluate the safety and efficacy of perioperative steroids for infant heart surgery with CPB.[13, 14, 16, 20]

4 TRIAL DESIGN AND METHODS

4.1 Overview

This study is a prospective, double-blind, multi-center, placebo-controlled safety and efficacy study of methylprednisolone in infants undergoing planned heart surgery with CPB. The study will enroll up to 1500 infants (< 1 year of age) including a minimum of 400 neonates ≤ 30 days at the time of surgery. The total study duration is expected to be approximately 48 months. An ancillary PK/PD/Biomarker study will enroll subjects at select centers. This study is unique in that it is designed to leverage existing registry infrastructure at participating sites so as to reduce trial costs. Participants will be randomized and will receive a subject ID. This ID will also serve as a unique patient identifier allowing us to crosslink datasets. Participants will then receive study drug/placebo administered into the pump prime during cardiopulmonary bypass. All study participants will then receive routine post-operative care. Participating centers will enter all demographic, preoperative, operative and outcomes data into their existing institutional databases for submission to the STS-CHSD as they currently do. These data will be used to evaluate trial outcomes.

4.2 Procedures to Minimize/Avoid Bias

4.2.1 Randomization

Eligible participants will be randomized prior to their electively scheduled surgery in a 1:1 fashion to the treatment groups summarized in table 2 below. A block randomization scheme will be employed to ensure equal allocation by study site. Randomization assignments will be generated by a web-based system at the data coordinating center (DCC), after confirmation of trial eligibility. Trial sites will enter the randomization number into two databases that will be used for this trial (see section 6.4): the participating center's surgical database (for submission to the STS-CHSD), and an IBM Clinical Development database that will be used to capture some adverse event data, timing of drug delivery and timing of PK samples (for participating centers only) and a subset of laboratory values from the electronic health record.

Table 1. Study Drug dosing

Group	N	Intra-operative
1	up to 750	IV methylprednisolone in the CPB prime
2	Up to 750	Placebo

4.2.2 Blinding

The study medication and the placebo will be identical in appearance to assure masking of study medication. The randomization assignment will be seen only by the statistician at the DCC and the investigational pharmacist preparing the study medication. The family/subject, study coordinator and investigators will remain masked as to treatment group assignment until after all trial data are analyzed.

4.3 Study measures

Study outcomes were determined after trial simulations. Based upon these data we selected the following primary and secondary outcome measures.

4.3.1 Primary Endpoint

A composite mortality, major morbidity and length of stay global rank endpoint with endpoints ranked according to severity. The global rank score has been previously described.[23] Subjects will receive a rank score based upon the lowest ranking (worst) endpoint that they experience during the study trial.

Table 2. Global Rank Endpoint Details

Rank Score	Description
1	Operative mortality
2	Heart transplant (during hospitalization)
3	Renal failure with permanent dialysis, neurologic deficit persistent at discharge, or respiratory failure requiring tracheostomy
4	Post-operative mechanical circulatory support or unplanned cardiac reoperation (exclusive of reoperation for bleeding)
5	Reoperation for bleeding, delayed sternal closure, or post-op unplanned interventional cardiac catheterization
6	Post-op cardiac arrest, multi-system organ failure, renal failure with temporary dialysis, or prolonged ventilator support (> 7 days)
7	Post-operative length of stay > 90 days
8-97	Post-operative length of stay

4.3.2 Secondary Endpoints (see section 11.2 for data element definitions)

Efficacy:

- Mortality including in-hospital mortality or mortality after hospital discharge but within 30 days of the last dose of study drug
- Death or major complication as defined by an outcome in one of the 6 highest global ranking categories
- Post-operative hospital length of stay
- Prevalence of prolonged (> 7 days) post-operative mechanical ventilation

- Occurrence of post-operative low cardiac output syndrome

Safety:

- Occurence of any one or more of the following STS-CHSD-defined major post-operative infectious complications:
  - Postprocedural infective endocarditis
  - Pneumonia
  - Sepsis
  - Deep wound infection
  - Mediastinitis
- Other post-operative complications will be collected from the start of study drug/placebo administration until hospital discharge.

PK/PD/Biomarkers:

- Time to maximum concentration (T_{max})
- Maximum concentration (C_{max})
- Clearance (CL)
- Volume of distribution (Vd)
- Post-operative blood markers of inflammation

PK/PD and Biomarker data will only be collected at select centers and in those patients whose parent/legally authorized representative have granted consent to blood draws. An opt in/out clause is included in the informed consent forms for study participants and centers will be allowed to participate in this part of the study if they prefer. Parent/legally authorized representative of participants may elect to participate in the PK/PD, the Biomarker studies or both. Time points for blood collection will be the same for both the PK/PD and biomarker studies. Biomarkers being collected represent blood markers of inflammation.

4.3.3 Timeframe for collection of safety and efficacy endpoints

With respect to primary and secondary outcome measures, participants will be followed for the duration of their hospitalization. Data will be collected consistent with standard STS-CHSD reporting protocol. Participants that are discharged within the first 30 days after their initial cardiac surgery, or any participants that receive study drug/placebo but then do not undergo surgery, will be followed to assess for mortality through 30 days after administration of study drug/placebo. If patients remain hospitalized for > 4 months after the final study subject has been enrolled then they will be assigned the worst rank outcome that they have encountered to that point. Patients still hospitalized with mechanical circulatory support and listed for heart transplant will assigned to the "heart transplant" outcome (See missing data section for exceptions). Serious study drug-related adverse events will be collected through 7 days after administration of study drug. Based upon an 18 hour estimated half- life of methylprednisolone, this duration of follow up (> 10 half-lives) will ensure collection of all potentially study drug-related serious adverse events but avoids capturing unnecessary serious adverse events in this high morbidity patient population.

4.4 Schedule of events

Participants will be enrolled at the time of their electively scheduled surgery. Sites will receive a randomization ID that will be entered into the two relevant databases: the sites' surgical database (STS-

CHSD), and an IBM Clinical Development clinical database. The study drug/placebo will be administered in the CPB pump prime at the time of initiation of CPB. Participants will then undergo surgery with CPB per standard of care. Participants will receive routine post-operative care. Post-operative outcomes including post-operative hospital length of stay, discharge mortality, and complication data will be recorded in the sites institutional surgical database (STS-CHSD) consistent with current practices at the enrolling sites. STS-CHSD data element definitions of particular relevance to the STRESS trial are included in Section 11.2. A subset of additional safety endpoints and select safety laboratory values from the electronic health record will be collected into a separate clinical database, IBM Clinical Development (see section 6.4). Plasma samples including PK/PD/Biomarker samples will be evaluated in a subset of enrolled patients at select centers using a limited sampling scheme. Sample acquisition, handling, and shipping instructions are outlined in Appendix C.

Table 3. Schedule of events

Procedure	Pre-dose	Day 1	Day 2	Day 3	Day 4-7	Duration of hospitalization[3]
Informed Consent	X					
Demographics	X					
Physical Exam	X					
Medical History	X					
Elective surgery with CPB		X				
Administer study drug/placebo[1]		X				
Timed PK/PD/Biomarker Samples[2]		X	X			
Study drug-related SAEs	X	X	X	X	X	
STS-CHSD data (1° / 2ndary endpoints)		X	X	X	X	X

[1] Study drug/placebo will be administered at the time of initiation of CPB

[2] Specific times of PK/PD/Biomarker sampling TBD based upon preliminary analysis of an on-going population PK study

[3] Mortality data will be collected for the duration of hospitalization or until 30 days after study drug / placebo administration for patients that are discharged. If patients remain hospitalized for > 4 months after the final study subject has been enrolled then mortality data for the hospitalization will not be collected and they will be assigned the worst rank outcome that they have encountered to that point.

5 SELECTION AND WITHDRAWAL OF SUBJECTS

5.1 Inclusion criteria

1. Age < 1 year at the time of surgery
2. Planned heart surgery with CPB as part of standard clinical care.
3. Availability and willingness of the parent/legally authorized representative to provide written informed consent.

5.2 Exclusion criteria

1. < 37 weeks adjusted gestational age at time of surgery
2. Any oral or intravenous steroid treatment within two days of surgery
3. Any patient receiving any of the following medications within 2 days of surgery: Amphoteracin B, aminoglutethimide, anticholesterases, warfarin, P450 3A4 inducers

including (but not limited to) carbamazepine, phenobarbital, phenytoin, rifampin, bosentanand nafcillin or P450 3A4 inhibitors including (but not limited to) clarithromycin, voriconazole, itraconazole, ketoconazole, ciprofloxacin, diltiazem, fluconazole, erythromycin, azithromycin and verapamil.

4. Infection contraindicating steroid use
5. Preoperative mechanical circulatory support or active resuscitation at the time of randomization
6. Previous enrollment in the STRESS trial

5.3 Subject withdrawal

Participants that are randomized but do not receive study drug/placebo before 1 year of life will be withdrawn from the study.

5.4 Recruitment/enrollment procedures protocol

Expected duration of accrual of subjects is approximately 48 months. Recruitment will be conducted using standard procedures. To help with recruitment, information describing the study will be developed for print, electronic, and social media. Subjects' parent/guardian will be approached for participation, either in person or by telephone, by site study coordinators or investigators, who will obtain parental consent following standard procedures. The specific procedures will be in compliance with the requirements of each site's Institutional Review Board.

6 STUDY PROCEDURES

6.1 Preoperative Assessment – Screening Procedures and Baseline Measurements

1. Obtain a signed and dated Informed Consent Form (ICF) prior to any study related procedures.
2. Enter all demographic, preoperative risk factor and past medical/surgical history data into the STS-CHSD as per routine
3. Obtain a unique subject ID from the IBM Clinical Development database. This subject ID will also serve as a unique patient identifier allowing cross-linking across databases. It must also be entered into the site's surgical database under the study identifier tab as the "STS-related clinical trial ID" (see section 6.4). In addition the STS "Operation ID" must be entered into both databases and will serve as a double check in the event that the IBM Clinical Development subject ID is incorrectly entered into either of the 2 databases.
4. Perform routine preoperative assessment

6.2 Baseline/Pre-Dose Assessment

After the parent or legally authorized representative has signed the IRB-approved informed consent form, and after it has been determined that the patient satisfies all inclusion and exclusion criteria, the following evaluations will be performed and entered directly into the study database (STS-CHSD):

1. Baseline demographics (race, gender, date of birth, age, weight, age and weight at surgery)

2. Fundamental cardiac diagnosis as defined by the STS-CHSD
3. Presence of any of the 41 STS-CHSD defined preoperative risk factors including mechanical ventilation to treat cardiorespiratory failure, sepsis, stroke, renal failure or hepatic dysfunction as defined by the STS-CHSD.
4. Presence of any non-cardiac anatomic abnormality, genetic syndrome or chromosomal anomaly as defined by the STS-CHSD.

6.3 Study Procedures During Study Drug Administration

The following procedures or evaluations will be performed during and immediately following the drug administration and the data recorded as indicated:

1. Record study drug/placebo dosing information including dose and timing of drug administration into the IBM Clinical Development database.
2. Immediately (within 1 business day of first becoming aware of the adverse event) enter all serious, study drug-related adverse events into the IBM Clinical Development database.

6.4 Study Procedures After Study Drug Administration During Hospitalization

The following information will be collected using the standard STS-CHSD data collection forms consistent with usual institutional practice:

1. Record all post-operative complications using standard STS-CHSD data element definitions (see section 11.2 for definitions)
2. Record all subsequent surgeries (CPB or non-CPB cardiovascular or non-cardiovascular)
3. Record duration of mechanical ventilation
4. Record post-operative hospital length of stay
5. Record operative mortality (in-hospital death or death after hospital discharge but within 30 days of the surgery/administration of study drug/placebo)

All other aspects of care, including administration of clinically indicated medications can be provided per routine standard of care.

Serious, study drug-related adverse events may require expedited reporting and must be submitted into the IBM Clinical Development database. Sites must report these events within 1 business day of first becoming aware of the event.

The variables listed in Table 4 are not collected by the STS-CHSD and will need to be collected directly from the Electronic Health Record. These variables must be entered directly into the relevant databases as specified in Table 4.

Table 4: Additional variables to be captured from the electronic health record

Variable	Definition	Database
Post-operative highest blood glucose	Enter the highest post-operative blood glucose within 72hrs of surgery	IBM Clinical Development
Post-operative insulin administration	Was insulin administered within 24 hours of surgery?	IBM Clinical Development
Post-operative adrenal suppression	Was hydrocortisone administered within 72 hours of surgery?	IBM Clinical Development
Preoperative creatinine	Enter the last serum creatinine level obtained prior to surgery	IBM Clinical Development

Highest post-operative creatinine	Enter the highest serum creatinine within 72 hours of surgery	IBM Clinical Development
Lowest post-operative potassium	Enter the lowest post-operative potassium within 72 hours of surgery	IBM Clinical Development
Highest post-operative AST	Enter the highest AST within 72 hours of surgery	IBM Clinical Development
Highest post-operative ALT	Enter the highest ALT within 72 hours of surgery	IBM Clinical Development
Highest post-operative lactate	Enter the highest lactate within 72 hours of surgery	IBM Clinical Development
Lowest post-operative serum cortisol	Enter the lowest serum cortisol level obtained within 72hrs of surgery	IBM Clinical Development

6.5 PK/PD/Biomarker sampling procedures (select sites)

A limited PK/PD/Biomarker sampling scheme will be employed such that no more than 5600 µl (7 samples, 800 µl per sample) of blood is obtained (Table 5). Blood samples will be collected in 800 µL aliquots. Children who have only 1 evaluable PK sample will be included in the analysis, but additional participants may be enrolled to ensure at least 100 children with < 4 adequate PK samples.

Table 5. PK/PD/Biomarker sampling scheme

Sample Number	Per Patient Prioritization	Time	Per patient blood collection
1	Please always try to collect this	Pre-dose (biomarker only)	4 x 200 uL = 800 uL
2	Collect a minimum of 2 of any of these 5 time points to collect a minimum total of 3 time points per participant.	0-30 minutes after the start of CPB	4 x 200 uL = 800 uL 4 x 200 uL = 800 uL
3		0-30 minutes after MUF	
4		1-2 hours after completion of CPB	
5		4-6 hours after completion of CPB	
6		16-24 hours after completion of CPB	
7	If participating in the biomarker arm, then please always try to collect this	36-48 hours after completion of CPB	4x 200 uL = 800 uL

Timed PK/PD/Biomarker sample handling procedures (plasma):
Assays to measure methylprednisolone concentrations and measures of the inflammatory response to CPB in plasma will be conducted at a central lab using validated bioanalytical assays. The date and time will be recorded for the administration of study drug/placebo, and the acquisition time of the PK sample.

7 TREATMENTS TO BE ADMINISTERED

7.1 Description of Study Treatments

Eligible subjects will be randomized prior to their electively scheduled surgery in a 1:1 fashion to methylprednisolone (30mg/kg) versus placebo as summarized in table 2 above. The dosages for administration (30 mg/kg) are based upon expert consensus regarding current practice and a previous dosing study. Intravenous methylprednisolone is available in a **preservative free** single use "Act-O-Vial

System" containing powder (40mg, 125mg, 500mg and 1000mg options are available) and diluent. Study drug will be provided "off the shelf" by study sites and prepared following local pharmacy protocols. Only preservative-free solutions will be used for this trial due to safety concerns with the administration of benzyl alcohol preservatives in infants. Study drug will be mixed with isotonic saline in a syringe to create a solution. Placebo preparations will consist of isotonic saline only and will be prepared in identical syringes so as to be physically indistinguishable from study drug.

7.2 Route of Administration

For the purposes of this trial methylprednisolone will be administered as a bolus dose administered directly into the CPB priming solution (intraoperative administration).

7.3 Storage and Administration

Study drug/placebo will be prepared by the site investigational pharmacy and delivered to the operating room from the investigational pharmacy on the day of study drug/placebo administration. All co-investigators, staff administering study drug/placebo and other care providers will be blinded to study drug/placebo allocation. Start and stop times of study drug administration must be documented by the investigational pharmacy in the IBM Clinical Development database.

8 STUDY DRUG ACCOUNTABILITY

8.1 Medications/Treatments Permitted and Not Permitted during the Study

8.1.1 Rescue Medication, Emergency Procedures and Additional Treatments(s)

Management would be symptomatic treatment (e.g., severe hypertension) or observation and monitoring (e.g., mild hyperglycemia).

8.1.2 Restrictions regarding concomitant treatment

Subjects may be treated with other medications at the discretion of their physicians.

8.2 Emergency Unblinding

An emergency code break can be requested from the site research pharmacist after full discussion with the STRESS PI. This code break may be used in rare life-threatening or emergency situations when the identity of the study drug must be known to the investigator in order to provide appropriate medical treatment or if required to assure safety of trial participants. If the code break for a subject is required, the DCC must be informed within one working day of the event. The reason for breaking the code will be documented by the Data Coordinating Center (Duke Clinical Research Institute) accordingly.

9 SAFETY ASSESSMENTS AND MONITORING

9.1 Collection and Reporting

Due to the unique study design, adverse events will be recorded by the site as complications and/or other adverse event data variables specifically captured by the site's surgical database using STS-CHSD data element definitions (see Section 11.2).

Serious, study drug-related adverse events will be reported by site investigators or qualified designee from the time of study drug administration through 7 days after study drug administration on the SAE eCRF in the IBM Clinical Development database within 1 business day of first becoming aware of the event. The site investigator's reported relationship assessment to study drug will be confirmed or assessed otherwise by a Safety Medical Monitor at the Duke Clinical Research Institute.

9.2 Definitions of Adverse Events (AEs), Suspected Adverse Reaction and Serious Adverse Events

The FDA Final Rule on IND Safety Reporting Requirements [http://edocket.access.gpo.gov/2010/pdf/2010-24296.pdf] provides the following definitions:

Adverse events (AEs) An AE is any untoward medical occurrence associated with the use of a drug in a subject whether or not considered drug- or biologic-related. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a pharmaceutical product or biologic.

A **suspected adverse reaction (SAR)** is any adverse event for which there is a reasonable possibility that the drug caused the adverse event. A "reasonable possibility" suggests there is a causal relationship between the drug and the adverse event. "Suspected adverse reaction" implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

Serious adverse events: An adverse event or suspected adverse reaction is considered serious if, in the view of either the site investigator or the IND sponsor, it results in any of the following outcomes:

1. Death
2. Life-threatening AE: Places the subject at immediate risk of death at the time of the event as it occurred. It does not include an AE that, had it occurred in a more severe form, might have caused death.
3. Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
4. Inpatient hospitalization or prolongation of existing hospitalization

An important medical event that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, it may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in the definition above. This determination is based on the opinion of either the investigator or sponsor (e.g., if either believes it is serious, it must be considered serious).

Laboratory abnormalities are not specifically captured by institutions as part of their STS-CHSD and will not be considered AEs unless they result in a post-operative complication that sites report to the STS-CHSD. In this case, the clinical diagnosis rather than the laboratory term will be used by the reporting investigator (e.g., renal failure versus elevated creatinine).

9.3 Assessment of Severity

The determination of severity rests on medical judgment of a medically qualified investigator. For adverse events captured by the site's surgical database, the data monitoring committee will review these events every 6-months following transfer of data to the data coordinating center at the Duke Clinical Research Institute. For suspected unexpected serious adverse reactions, monitoring will be performed continuously and event severity will be graded by the study sponsor. The severity of suspected adverse reactions and study drug related SAEs will be graded using the following definitions:

1. MILD: Participant is aware of symptoms or has minor findings but tolerates them well and no or minimal intervention required.
2. MODERATE: Participant experiences discomfort enough to cause interference with usual activity and may warrant intervention.
3. SEVERE: Participant experiences symptoms that are incapacitating with inability to do usual activities or that significantly affect clinical status and warrant intervention.

Study personnel will enter the study drug-related serious adverse event data into the IBM Clinical Development database. The STRESS Trial PI / IND sponsor will be responsible for adjudicating severity and relatedness of these events and determining which events should be reported in expedited fashion to FDA. The IND sponsor or designee will submit expedited safety reports (IND Safety Reports) to the FDA and other regulatory agencies as necessary, and will inform the investigators of such regulatory reports. Investigators must submit safety reports as required by their Institutional Review Board (IRB). Documentation of the submission to and receipt by the IRB should be retained for each IND safety report.

9.4 Assessment of Causal Relationship

A medically qualified investigator must assess the relationship of any adverse event to the use of the study drug, based on available information using the following guidelines:

1. **Not related**: There is not a reasonable causal relationship to the investigational product and the adverse event.
2. **Unlikely related**: No temporal association, or the cause of the event has been identified, or the drug or biologic cannot be implicated.
3. **Possibly related**: There is reasonable evidence to suggest a causal relationship between the drug and adverse event.
4. **Related**: There is evidence to suggest a causal relationship, and the influence of other factors is unlikely.

Relatedness to these complications will not be specifically assigned by the Data Monitoring Committee unless they are separately reported as suspected unexpected serious adverse reactions (SUSARs).

Expectedness

The expectedness of an adverse event or suspected adverse reaction shall be assessed by a DCRI Safety Medical Monitor according to the package insert. Any AE that is not identified in nature, severity, or specificity in the current package insert is considered unexpected. Events that are not mentioned in the

package insert as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but not specifically mentioned as occurring with the particular drug under investigation, are considered unexpected.

9.5 Identification of Safety Events

As subjects in this study may have pre-existing medical conditions and will be currently hospitalized, those pre-existing conditions will not be considered as adverse events unless they worsen or increase in frequency or intensity after administration of study drug. New events that occur or the worsening in frequency or intensity of pre-existing conditions will be reported as adverse events or, if serious reporting criteria are met, serious adverse events. Events that do *not* qualify as a study drug-related serious adverse event for the STRESS trial and should not be recorded in the IBM Clinical Development clinical database are:

- Medical or surgical procedures (e.g. surgery, transfusion); however, the condition that required the procedure is considered an adverse event if the situation developed or worsened due to study drug administration
- Pre-existing diseases or baseline conditions present or detected before the start of study drug that do not worsen in frequency or intensity due to study drug administration.
- Any events considered to be related to the patients underlying heart disease or recovery from his/her cardiac surgery, including any of the post-operative complications listed in the STS-CHSD.
- Serious Adverse Events that are assessed by the site investigator as Not related or Unlikely related to study drug

9.6 Safety Monitoring

The data coordinating center (DCC) will monitor safety during the conduct of the study. The study sponsor will review all potential unexpected study drug related serious adverse events at the time of SAE notification by DCRI Safety Surveillance and confirm whether the event is a suspected unexpected serious adverse reaction (SUSAR). The data monitoring committee (DMC) will monitor safety every 6 months as per the DMC charter. Annual and expedited reports will be submitted to the FDA as required.

9.7 Halting Rules

All patients who receive study medication will be followed for safety. An independent data monitoring committee consisting of three physicians will conduct an internal review of study safety every 6-months of study enrollment. The safety review will include all SAEs and all AEs captured in either the STS-CHSD or the separate IBM Clinical Development clinical database that the data monitoring committee determine are possibly or probably related to the study drug and all patients who discontinued participation in the study early. If >3 subjects experience **active** (not placebo) **study drug-related** SAEs of the same Preferred Term (MedDRA coding), the DMC will be notified. Decisions to halt the trial will be at the discretion of the DMC.

If the study is halted, the AEs will be thoroughly evaluated and study enrollment will not resume until the safety review is completed.

9.8 Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multi-Center Clinical Trials

The site Investigator or designee is responsible for reporting all serious adverse events to the local IRB/REB in accordance with local policies and procedures.

9.9 Follow-up of Subjects after Adverse Events

For Serious AEs with a positive causal relationship to the study drug, follow-up by the investigator is required until the event or its sequelae resolve or stabilize at a level acceptable to the investigator.

9.10 Study Suspension

Study enrollment and administration of study drug/placebo will be stopped for a safety review based upon the recommendations of the DMC.

10 STATISTICS

10.1 Planned Sample Size

The trial's sample size was formulated to provide high power (>90%) for detecting a clinically important treatment benefit in patients randomized to steroids versus placebo as measured by the trial's primary global ranking endpoint categories with testing based on the Wilcoxon rank sum test or, equivalently, the proportional odds logistic regression model score test [24]. The magnitude of the hypothesized treatment effect of steroids versus placebo was quantified by the win difference $P_1 - P_0$ where P_1 is the probability that a randomly selected patient in the steroids group will have a better outcome (higher global ranking category) than a randomly selected patient in the placebo group and P_0 is the probability that a randomly selected patient in the steroids group will have a worse outcome (lower global ranking category) than a randomly selected patient the placebo group. As shown in Table 6, a sample size of approximately 1,200 participants will provide approximately 85% power if the win difference is 0.10 and will provide 95% power if the win difference is 0.12. Thus, the study has good power to detect a meaningful improvement in the probability of a better outcome with steroids compared to placebo. For an alternative perspective on the study's power, the treatment effect of steroids versus placebo may be quantified by specifying the extent to which the odds of having an outcome in one of the k lowest (worst) global ranking categories is reduced in patients randomized to steroids versus placebo, where $k \leq 1$ refers to the odds of death, $k \leq 2$ refers to the odds of death or heart transplant, etc. Specifically, the treatment effect may be quantified by the set of odds ratios

$$OR_{\leq k} = \frac{\text{odds of having an outcome in category } \leq k \text{ if randomized to steroids}}{\text{odds of having an outcome in category } \leq k \text{ if randomized to placebo}}, k = 1,2,\ldots,96,$$

where for simplicity we may assume that $OR_1 = OR_2 = \cdots = OR_{96} (\equiv OR)$. As shown in Table 6, a sample size of 1,200 participants will provide approximate 82% power if the odds ratio is 0.75 (i.e. a 25%

reduction in the odds) and approximately 95% power if the odds ratio is 0.70 (i.e. a 30% reduction in the odds). Thus, the study is well powered under a range of clinically relevant and plausible risk reduction scenarios. For simplicity, power statements above are based on approximate power using a Wilcoxon test ignoring baseline covariates. However, to increase statistical power, analysis of the primary endpoint will be adjusted for baseline covariates, as described in Section 10.3 below. Based on Monte Carlo simulations, a covariate adjusted analysis will increase power by an amount ranging from 3 to 5 percentage points compared to an unadjusted analysis under assumptions consistent with 80%-90% power for the unadjusted analysis.

Table 6. Estimated power as a function of the effect size as quantified by the win difference or odds ratio assuming N = 1,200 (600 per group)

Effect Size Parameter	Win Difference ($P_1 - P_0$)			Odds Ratio (OR)		
Numerical Effect Size	**0.10**	**0.11**	**0.12**	**0.75**	**0.725**	**0.70**
Power (N = 1,200)	85%	91%	94%	82%	90%	95%

Assumptions: Based on two-sided alpha=0.05. Power was calculated as $\Pr[X^2_{n\Delta} > 3.841]$ where $X^2_{1,n\Delta}$ denotes a chi-squared random variable with 1 degree of freedom and non-centrality parameter $n\Delta$, where $n = 1200$ and $\Delta = 3(P_1 - P_0)^2/(4\rho)$ (derived from formulas in Zhao et al.[24]) or $\Delta = \log(\mathrm{OR})/(12/\rho)$ (derived from formulas in Whitehead [26]) where ρ is the probability that 3 randomly selected trial participants will not all have outcomes in the same global ranking category. The quantity ρ reflects the reduction in variance due to ties and was set to its maximum possible value ($\rho = 1$) in order to obtain a conservative lower bound approximation of power for a specified win difference. Calculations do not account for an expected slight loss of power after decreasing alpha to account for interim analyses.

10.2 Statistical Analysis Plan

All major treatment comparisons between the randomized groups will be performed according to the principle of "intention-to-treat"; that is, subjects who received study drug/placebo will be analyzed (and endpoints attributed) according to the group to which subjects were randomized, regardless of subsequent medications or treatment crossover. Statistical comparisons will be performed using 2-sided significance tests.

10.3 Analysis of the Primary Endpoint

The trial's global ranking endpoint outcome is an ordinal categorical variable having K levels, where category 1 represents the worst possible outcome (e.g. death) and category K represents the best possible outcome (e.g. a short hospital stay free of death or major complications) according to a pre-specified subjective global ranking algorithm (see above). Table 7 summarizes the distribution of ranking endpoints in neonates and infants in a historical cohort of patients from the STS database. The actual observed distribution of ranking categories in the trial will be compared across treatment groups using a stratified non-parametric Wilcoxon rank sum test (also known as the van Elteren test [27]) with stratification by categories of pre-randomization predicted mortality or morbidity risk or by using a regression-based analog of the van Elteren test which allows adjusting for multiple pre-randomization prognostic factors in order to maximize statistical power [28]. Covariates for stratification or covariate adjustment will be determined prospectively and will be pre-specified in the statistical analysis plan. The level of

significance for the assessment of the primary endpoint will be α=0.05 (two-sided). The magnitude of the treatment effect will be described by presenting summary measures of the frequency distribution of ranking categories by treatment group and by estimating the probability that a randomly selected steroids group participant will have a better or worse outcome than a randomly selected placebo group participant (e.g. the win ratio [29]). If the data provide evidence of an overall difference in outcome between treatment groups, we will further examine whether the therapeutic effect is similar for all participants, or whether it varies according to specific participant characteristics, which will be pre-specified in the statistical analysis plan. These analyses will use ordinal regression models and will involve testing for interactions between treatment and these specific baseline variables. Effect estimates for subgroups will be carefully (conservatively) interpreted in conjunction with the formal interaction tests.

Table 7. Cumulative frequency of endpoints included in the global rank outcome

Global Rank Endpoints	Age ≤ 30d	Age < 1yr
Operative mortality	8.9%	4.5%
Heart transplant (during hospitalization)	9.2%	5.4%
Renal failure with permanent dialysis, neurologic deficit persistent at discharge, or respiratory failure requiring tracheostomy	10.8%	6.6%
Post-operative mechanical circulatory support or unplanned cardiac reoperation (exclusive of reoperation for bleeding)	19.2%	11.8%
Reoperation for bleeding, delayed sternal closure or post-op unplanned interventional cardiac catheterization	27.1%	16.7%
Post-op cardiac arrest, multi-system organ failure, renal failure with temporary dialysis, or prolonged ventilator support (> 7 days)	36.1%	21.9%
Prolonged post-op length of stay (> 90 days, binary endpoint)	36.6%	22.3%

*Data compiled from the STS Congenital Heart Surgery National Registry (2010-2015)

10.4 Analysis of Secondary Safety and Efficacy Endpoints

Secondary endpoints will be analyzed via regression modeling with adjustment for pre-randomization covariates. For secondary endpoints that are binary (e.g. mortality, composite mortality or major complications, low cardiac output syndrome), the form of the model will be a logistic regression comparing the endpoint event rate across the two treatment groups. For continuous outcomes with skewed distributions (e.g., post-operative hospital length of stay, duration of mechanical ventilation) the outcome will be approximated by a skewed distribution such as log-normal, Weibull or negative binomial, or modeled semi-parametrically. For safety analyses, we will summarize the number of adverse events overall, by severity, and by each Medical Dictionary for Regulatory Activities system organ class and preferred term. We will tabulate adverse event data by procedural risk cohort (STAT levels).

10.5 Interim Analyses

Interim examination of clinical endpoints and key safety events will be performed at regular intervals during the course of the trial. An independent Data Monitoring Committee (DMC) will monitor participant safety and review performance of the trial. The primary objective of these interim analyses will be to ensure the safety of the participants enrolled in the trial and evaluate the accumulating endpoint data by treatment group to test for possible differences favoring either

of the two randomized management strategies. In addition, interim monitoring will involve a review of participant recruitment, compliance with the study protocol, status of data collection, and other factors which reflect the overall progress and integrity of the study.

Formal interim treatment group comparisons will focus on comparing the distribution of the primary global ranking endpoint categories by treatment group. To account for repeated significance testing of the accumulating data, the group sequential method of Lan and DeMets will be used as a guide for interpreting these interim analyses. Monitoring boundaries for the primary endpoint will be based on a two-sided symmetric O'Brien-Fleming type spending function with an overall two-sided significance level of $\alpha = 0.05$. The O'Brien-Fleming approach requires large critical values early in the study but relaxes (i.e., decreases) the critical value as the trial progresses. These proposed monitoring boundaries are intended as a guide for interpreting the interim analyses and not as a strict rule for early termination. The first interim analysis using alpha spending will be targeted to occur after completion of data collection for the first ~600 to 800 subjects depending on timing of the STS data harvest. Additional interim analyses will be performed at intervals determined by the DMC. Study enrollment will be allowed to continue pending compilation of the interim data and review/recommendations from the DMC.

Update 15 September 2020: Due to a delay in receiving the STS-CHSD data harvest, the DMC Chair is agreeable to proceed with the interim analysis in the following manner. The unblinded statistical team will plan to access and compile Length of Stay (LOS) and mortality data by treatment allocation from the IBM Clinical Development clinical database. This data will be reviewed by the DMC during a convened DMC meeting. If these data suggest any safety concerns, the study team will proceed with the previously planned interim analysis whenever the STS-CHSD data are available. If there are no identified safety concerns then enrollment will continue to trial completion.

10.6 Data Monitoring Committee

A DMC will be appointed by the trial's leadership to monitor participant safety and to review performance of the trial. A DMC charter that outlines the operating guidelines for the committee and the procedures for the interim evaluations of study data will be developed by the trial's leadership and agreed upon by the DMC. Reports will be prepared regularly in accordance with the plan outlined in the charter and as requested by the DMC chair, and will include interim analyses of primary and secondary endpoints; additional safety events; and other information as requested by the committee. After each meeting, the DMC will make recommendations to the trial's leadership about the continuation of the study. After approval by trial leadership, a summary of the DMC report and recommendations will be forwarded to site investigators for submission to their local IRB.

10.7 Population for Analysis

- Efficacy: All participants who receive study drug/placebo.
- Safety: All participants who receive study drug/placebo.
- PK/PD/Biomarkers: All participants who receive methylprednisolone and have at least 1 evaluable PK sample.

11 DATA MANAGEMENT

11.1 Data entry

The majority of data for the STRESS trial will be captured via the STS-CHSD. Sites must enter the IBM Clinical Development subject ID into the participating subjects STS-CHSD record under the "STS-related clinical trial ID" tab/variable. This identifier must be entered into the STS database immediately after it is assigned. This identifier will be used to link the two databases. For other variables, the STS-CHSD includes specific data element definitions that must be closely followed (see section 11.2).

Serious, unexpected, study drug-related adverse events may require expedited reporting and therefore must be collected in an expedited fashion. Since the STS-CHSD data are only harvested every 6-months, a separate IBM Clinical Development database has been developed to capture these events. Study drug-related serious adverse events must be submitted into the IBM Clinical Development database within 1 business day of first becoming aware of the event. The IBM Clinical Development database will also be used to capture a select subset of additional variables including timing of medication administration, adverse events of interest that are felt to be study drug-related (see section 9.2) and timing of PK/PD/Biomarker sample collection (for participating sites).

In addition, a small subset of select post-operative laboratory administration variables (Table 4) need to be captured but are not incorporated into the STS-CHSD. These data must be collected from the electronic health record and the data entered directly into the IBM Clinical Development database.

As summarized above, the IBM Clinical Development subject ID will be used to link the two databases. As a safety control, sites will enter the STS "Operation ID" into the IBM Clinical Development database. In the event that the IBM Clinical Development subject ID is miss-entered into one of the databases, the STS Operation ID will be used to ensure accurate linkage.

11.2 Data Element Definitions

All STRESS data element definitions are based upon the STS-CHSD data element definitions which are available on-line at: http://www.sts.org/sites/default/files/documents/CongenitalDataSpecsV3_3_Updated.pdf. Some specific definitions of particular relevance to the STRESS trial are listed below:

Fundamental diagnosis: The fundamental diagnosis is a diagnosis that is carried with a patient throughout life, through all operations and hospitalizations. **The fundamental diagnosis is the most complex cardiac anomaly or condition (congenital or acquired) of the patient.** Most frequently, the primary diagnosis will also be the fundamental diagnosis. For some operations, however, the fundamental diagnosis and primary diagnosis will be different. For example, consider a child who underwent repair of subaortic stenosis, subsequently develops complete atrioventricular (AV) block, and undergoes pacemaker placement within the same hospitalization. The primary diagnosis for the pacemaker surgery is "Arrhythmia, Heart block, Acquired", while the fundamental diagnosis is "Aortic stenosis, Subvalvar". Similarly, a patient who has a complete AV canal defect and undergoes either palliation or repair of the defect has a primary and fundamental diagnosis of "AVC (AVSD), Complete CAVSD". Subsequently, the child develops mitral insufficiency and is re-hospitalized for mitral valve replacement. The primary

diagnosis for the mitral valve replacement operation is “Mitral regurgitation”, but the fundamental diagnosis is “AVC (AVSD), Complete CAVSD.” The utilization of the fundamental diagnosis field, it is hoped, will clarify designation of a primary diagnosis, and enable greater specificity in the lesion specific report analyses.

STS-CHSD data element definitions for primary outcome measures:

Death: For the purposes of STRESS, we will use the following definition of operative mortality which includes: (1) all deaths, regardless of cause, occurring during the hospitalization in which the operation was performed, even if after 30 days (including patients transferred to other acute care facilities); and (2) all deaths, regardless of cause, occurring after discharge from the hospital, but before 30 days after administration of study drug/placebo.

Heart transplantation: Includes any technique, allograft or xenograft.

Renal failure requiring permanent dialysis at discharge: Renal failure - acute renal failure (ROOT Definition) + with new postoperative/postprocedural requirement for dialysis, including peritoneal dialysis and/or hemodialysis. Code this complication if the patient requires dialysis at the time of hospital discharge or death in the hospital. (This complication should be chosen only if the dialysis was associated with acute renal failure.) {"Renal failure - acute renal failure" ROOT Definition = Acute renal failure is defined as new onset oliguria with sustained urine output < 0.5 cc/kg/hr for 24 hours and/or a rise in creatinine > 1.5 times upper limits of normal for age (or twice the most recent preoperative/preprocedural values if these are available), with eventual need for dialysis (including peritoneal dialysis and/or hemodialysis) or hemofiltration. Acute renal failure that will be counted as an operative or procedural complication must occur prior to hospital discharge or after hospital discharge but within 30 days of the procedure. The complication is to be coded even if the patient required dialysis, but the treatment was not instituted due to patient or family refusal.

Neurological deficit persisting at discharge: Newly recognized and/or newly acquired deficit of neurologic function leading to inpatient referral, therapy, or intervention not otherwise practiced for a similar unaffected inpatient, with a persisting neurologic deficit present at hospital discharge. In other words, new (onset intraoperatively or postoperatively – or intraprocedurally or postprocedurally) neurological deficit persisting and present at discharge from hospital.

Respiratory failure, requiring tracheostomy: Failure to wean from mechanical ventilation necessitating the creation of a surgical airway.

Renal failure requiring temporary dialysis: Acute renal failure (ROOT Definition) + With new postoperative/postprocedural requirement for temporary dialysis, including peritoneal dialysis and/or hemodialysis. Code this complication if the patient does not require dialysis at the time of hospital discharge or death in the hospital. (This complication should be chosen only if the dialysis was associated with acute renal failure.) {"Renal failure – acute renal failure" ROOT Definition = Acute renal failure is defined as new onset oliguria with sustained urine output < 0.5 cc/kg/hr for 24 hours and/or a rise in creatinine > 1.5 times upper limits of normal for age (or twice the most recent preoperative/preprocedural values if these are available), with eventual need for dialysis (including peritoneal dialysis and/or hemodialysis) or hemofiltration. Acute renal failure that will be counted as an operative or procedural complication must occur prior to hospital discharge or after hospital discharge but within 30 days of the procedure.

Postoperative/Postprocedural mechanical circulatory support: Utilization of postoperative/postprocedural mechanical support, of any type (IABP, VAD, ECMO, or CPS), for resuscitation/CPR or support, during the postoperative/postprocedural time period. Code this complication if it occurs (1) within 30 days after surgery or intervention regardless of the date of hospital discharge, or (2) after 30 days during the same hospitalization subsequent to the operation or intervention.

Unplanned cardiac operation during the postoperative or postprocedural time period, exclusive of reoperation for bleeding: Any additional unplanned cardiac operation occurring (1) within 30 days after surgery or intervention in or out of the hospital, or (2) after 30 days during the same hospitalization subsequent to the operation or intervention. A cardiac operation is defined as any operation that is of the operation type of "CPB" or "No CPB Cardiovascular". The following operations will always be coded as "Planned Reoperation": (1) Delayed Sternal Closure, (2) ECMO Decannulation, (3) VAD Decannulation, (4) Removal of Broviac catheter. The following operations will always be coded as "Unplanned Reoperation": (1) Mediastinal exploration for infection, (2) Mediastinal exploration for hemodynamic instability, (3) Emergent mediastinal exploration for initiation of ECMO or VAD, (4) Reoperation for residual or recurrent lesion. Mediastinal exploration for bleeding is always coded separately as "Bleeding, Requiring reoperation".

Reoperation for bleeding: Postoperative/postprocedural bleeding requiring reoperation.

Unplanned non-cardiac reoperation: Any additional unplanned non-cardiac operation occurring (1) within 30 days after surgery or intervention in or out of the hospital, or (2) after 30 days during the same hospitalization subsequent to the operation or intervention.

Unplanned interventional cardiovascular catheterization procedure: Any unplanned interventional cardiovascular catheterization procedure occurring (1) within 30 days after surgery or intervention in or out of the hospital, or (2) after 30 days during the same hospitalization subsequent to the operation or intervention.

Cardiac arrest: A cardiac arrest is the cessation of effective cardiac mechanical function. This complication should be selected if the cardiac arrest developed after OR Entry Date and Time. Do not select this complication for patients under hospice care or DNR.

Multi-System Organ Failure: ***Note – this is the only complication variable where the STS-CHSD definition has been modified. The current STS-CHSD definition is non-specific therefore we have developed the following definition for specific use during the STRESS trial.***

Multi-system Organ Failure requires two or more of the following to be present:

- Neurologic dysfunction: any permanent or transient neurologic injury including clinical seizure
- Renal dysfunction: serum creatinine > 2 times baseline or temporary or permanent dialysis
- Hepatic dysfunction: AST or ALT > 2 times normal
- GI dysfunction: Any surgical or medically treated episode of Necrotizing enterocolitis
- Respiratory dysfunction: Mechanical ventilation > 7 days

Please code the individual organ system failures as well. If multi-system organ failure is associated with sepsis as well, please also code: "Sepsis, Multisystem Organ Failure".

STS-CHSD data element definitions for infectious complications

Pneumonia: A "respiratory disease characterized by inflammation of the lung parenchyma (including alveolar spaces and interstitial tissue), most commonly caused by infection". Pneumonia is diagnosed by appropriate clinical findings (such as fever, leukopenia or leukocytosis, and new onset of purulent sputum) and one or more of the following: positive cultures (of sputum or pulmonary secretions) and / or pulmonary infiltrate on chest x-ray. An endotracheal tube culture may or may not be positive. Patients commonly demonstrate an evolving area of focal lung consolidation accompanied by fever (>38.5). Pneumonia (pneumonitis) may affect an entire lobe (lobar pneumonia), a segment of a lobe (segmental or lobular pneumonia), alveoli contiguous to bronchi (bronchopneumonia), or interstitial tissue (interstitial pneumonia). These distinctions are generally based on x-ray observations.

Sepsis: Evidence of serious infection accompanied by a deleterious systemic response. In the time period of the first 48 postoperative or postprocedural hours, the diagnosis of sepsis requires the presence of a Systemic Inflammatory Response Syndrome (SIRS) resulting from a proven infection (such as bacteremia, fungemia or urinary tract infection). In the time period after the first 48 postoperative or postprocedural hours, sepsis may be diagnosed by the presence of a SIRS resulting from suspected or proven infection. During the first 48 hours, a SIRS may result from the stress associated with surgery and/or cardiopulmonary bypass. Thus, the clinical criteria for sepsis during this time period should be more stringent. A systemic inflammatory response syndrome (SIRS) is present when at least two of the following criteria are present: hypo- or hyperthermia (>38.5 or <36.0), tachycardia or bradycardia, tachypnea, leukocytosis or leukopenia, and thrombocytopenia.
Deep wound infection: A deep wound infection involves the deep soft tissues (e.g., fascial and muscle layers) of the incision AND the patient has at least ONE of the following numbered features: 1) Purulent drainage from the deep portion of the incision (but not from the organ / space component of the surgical site and no evidence of sternal osteomyelitis), 2) The deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has ONE of the following lettered signs or symptoms (unless the incision is culture negative): A) fever, B) localized pain, or C) tenderness, 3) An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination, or 4) A diagnosis of a deep wound infection by a surgeon or by an attending physician.

Wound infection-Mediastinitis: The diagnosis of mediastinitis must meet one of the following criteria: Criterion 1: Patient has organisms cultured from mediastinal tissue or fluid that is obtained during a surgical operation or by needle aspiration. Criterion 2: Patient has evidence of mediastinitis by histopathologic examination or visual evidence of mediastinitis seen during a surgical operation. Criterion 3: Patient has at least ONE of the following numbered signs or symptoms with no other recognized cause: 1) fever, 2) chest pain, or 3) sternal instability AND at least one of the following numbered features: 1) purulent mediastinal drainage, 2) organisms cultured from mediastinal blood, drainage or tissue, or 3) widening of the cardio-mediastinal silhouette. Criterion 4: Patient ≤ 1 year of age has at least one of the following numbered signs or symptoms with no other recognized cause: 1) fever, 2) hypothermia, 3) apnea, 4) bradycardia, or 5) sternal instability AND at least one of the following numbered features: 1) purulent mediastinal discharge, 2) organisms cultured from mediastinal blood, drainage or tissue, or 3) widening of the cardio-mediastinal silhouette. Infections of the sternum (sternal osteomyelitis) should be classified as mediastinitis. Sternal instability that is not associated with a wound infection or mediastinitis is documented as "Sternal instability".

Postprocedural infective endocarditis: Infective endocarditis in the setting of a heart which has been altered by surgery or intervention. Duke Criteria for the Diagnosis of Infective Endocarditis (IE): The definitive diagnosis of infective endocarditis requires one of the following four situations: 1) Histologic and/or microbiologic evidence of infection at surgery or autopsy such as positive valve culture or histology; 2) Two major criteria; 3) One major criterion and three minor criteria; 4) Five minor criteria. The two major criteria are: 1) Blood cultures positive for IE 2) Evidence of endocardial involvement. Blood cultures positive for IE requires: 1) Typical microorganism consistent with IE isolated from 2 separate blood cultures, as noted in number two below (viridans streptococci, Streptococcus bovis, Staphylococcus aureus, or HACEK group [HACEK, Haemophilus species {H. aprophilus and H. paraaphrophilus}, Actinobacillus actinoinycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.]) or (Community-acquired enterococci in the absence of a primary focus); 2) Microorganisms consistent with IE isolated from persistently positive blood cultures defined as: (At least 2 positive cultures of blood samples obtained > 12 hours apart) or (All of 3 or a majority of 4 or more separate cultures of blood, the first and the last sample obtained > 1 hr apart); 3) Single blood culture positive for Coxiella burnetii or an antiphase I IgG antibody titer of >1 :800. Evidence of endocardial involvement requires 1) Positive results of echocardiography for IE defined as: (Oscillating intracardiac mass on the valve or supporting structures in the path of regurgitant jets or on implanted material in the absence of an alternative anatomic explanation) or (Abscess) or (New partial dehiscence of a valvular prosthesis) or 2) New valvular regurgitation (worsening or changing or preexisting murmur not sufficient). The six minor criteria are: 1) Predisposing heart disease or injection drug use (IVDA); 2) Temperature of > 38C; 3) Vascular phenomenon (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial or conjunctival hemorrhage, Janeway's lesions); 4) Immunologic phenomenon (glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor); 5) Microbiologic evidence (a positive blood culture that does not meet a major criterion as noted above) or serologic evidence of active infection with an organism consistent with IE; 6) Echocardiographic findings that are consistent with IE but do not meet a major criterion as noted above. References: 1) Dhawan VK Infectious Endocarditis in Elderly Patients. Clin. Infect. Dis. 2002;34:806- 812. 2) Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. Am. J. Med. 1994;96:200-209. 3) Li IS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin. Infect. Dis. 2000;30:633-638. 4) http://gold.aecom.yu.edu/id/almanac/dukeendocarditis.htm, accessed July 5, 2006.

Select STS-CHSD data element definitions of particular relevance

Cardiac dysfunction resulting in low cardiac output: Low cardiac output state characterized by some of the following: tachycardia, oliguria, decreased skin perfusion, need for increased inotropic support (10% above baseline at admission), metabolic acidosis, widened Arterial – Venous oxygen saturation, need to open the chest, or need for mechanical support. If the cardiac dysfunction is of a severity that results in inotrope dependence, mechanical circulatory support, or listing for cardiac transplantation, please also code as "Cardiac failure (severe cardiac dysfunction)". A patient will be considered to have “inotrope dependence” if they cannot be weaned from inotropic support (10% above baseline at admission) after any period of 48 consecutive hours that occurs after the time of OR Exit Date and Time, and either (1) within 30 days after surgery in or out of the hospital, and (2) after 30 days during the same hospitalization subsequent to the operation. If patient meets criteria for severe cardiac dysfunction, only code "severe".

12 ETHICS AND HUMAN SUBJECTS CONSIDERATION

12.1 Institutional Review Board/Independent Ethics Committee Approval

Prior to its implementation, this protocol, including any subsequent amendments, must be IRB approved at each respective site, according to federal regulations.

12.2 Signed Informed Consent / Authorization

Prior to any study-related procedures, the investigator or designee will obtain from the patient's legally authorized representative (i.e., parent/legal guardian), a signed and dated written Informed Consent/Authorization consistent with FDA/ICH regulations, the HIPAA Privacy Rule. A HIPAA Privacy Rule Authorization language will be included in the Informed Consent/Authorization Form (where the Informed Consent and Authorization are combined in one document) and it will be IRB approved.

12.3 Duties of the Investigator

The investigator is obligated to conduct this study in accordance with U.S. federal regulation 21 CFR 312.60-69 as specified on the signed form FDA 1572, applicable state laws, and the International Conference on Harmonization: Good Clinical Practice: Consolidation Guideline. The investigator is responsible for informing the IRB of any safety issues related to the study and the study drug including reports of serious adverse events, if required, and all IND safety reports.

12.4 Records of the Study

A STS-CHSD will be used to record all patient data including all historical subject information and study data as specified by this protocol. The STS-CHSD data entry must be completed by designated and trained study personnel.

Source documents are defined as the results of original observations and activities of a clinical investigation. Source documents may include, but are not limited to, study progress notes, e-mail correspondences, computer printouts, laboratory data and recorded data from automated instruments.

It will be the responsibility of the Investigator(s) to assure that the study file at the site is maintained. The study file will contain, but will not be limited to:

- Current Package Insert and all previous versions over course of study
- Final study protocol
- Protocol Amendments (if applicable)
- Operations Manual (if applicable)
- Informed Consent Form (blank)
- Revised Informed Consent forms and/or all addenda (blank)
- DHHS Number for IRB or other documentation of IRB compliance with FDA regulations (if applicable)
- Documentation of IRB approval of protocol, consent form, any protocol amendments and any consent form revisions.
- Annual IRB updates and approvals
- All correspondence between the Investigator and IRB

12.5 Patient Privacy / Authorization

The principal investigator will ensure that the use and disclosure of protected health information obtained during a research study complies with the HIPAA Privacy Rule. The Rule provides U.S. federal protection for the privacy of protected health information by implementing standards to protect and guard against the misuse of individually identifiable health information of patients participating in Clinical Trials. “Authorization” is required from each research patient, i.e., specific permission granted by an individual to a covered entity for the use or disclosure of an individual’s protected health information. A valid authorization must meet the implementation specifications under the HIPAA Privacy Rule. Authorization will be combined in the Informed Consent document (approved by the IRB).

12.6 Informed Consent

Informed consent will be obtained and documented in accordance with U.S. 21 CFR Part 50.25, §§ 116, 117 and 408 of 45 CFR Part 46 and all other applicable regulatory requirements. Prior to any study procedures being performed, the investigator or his/her designee will inform the subject’s legally authorized representative (e.g., parent, guardian) of all aspects pertaining to study participation. Information should be given in both oral and written form whenever possible and deemed appropriate by the IRB. The subject’s legally authorized representative (parent or guardian) must be given ample opportunity to inquire about details of the study. The description of the study procedures will include the purpose of the research and procedures, risks and benefits of the research, alternative procedures, confidentiality, legal rights, parental or guardian permission, the contact person and phone number if there are any questions, and the voluntary nature of participation. It will be emphasized that participation is voluntary and participants may withdraw from the study at any time without any effect on standard care. Both the investigator or his/her designee, and the subject’s legally authorized representative must sign and date the informed permission form prior to the subject being enrolled in the study. An original signed informed consent will be retained in the site study records. The subject’s legally authorized representative will receive a copy of the signed and dated informed permission form and a copy of the signed assent (if applicable).

Permission forms must be in a language fully comprehensible to the subject’s legally authorized representative. Permission shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject’s legally authorized representative. The written parental/legal guardian permission document will embody the elements of informed consent as described in the Declaration of Helsinki, the Code of Federal Regulations, and the ICH Guidelines and will comply with local regulations. This form may be read to the subject’s legally authorized representative, but, in any event, the investigator shall give the representative adequate opportunity to read it before it is signed and dated. Permission must be documented by the dated signature of the subject’s legally authorized representative. The signature confirms the permission is based on information that has been understood. Each signed permission form must be kept on file by the investigators for possible inspection by Regulatory Authorities.

References

1. Petrini, J., K. Damus, and R.B. Johnston, Jr., *An overview of infant mortality and birth defects in the United States.* Teratology, 1997. **56**(1-2): p. 8-10.
2. Petrini, J., et al., *Contribution of birth defects to infant mortality in the United States.* Teratology, 2002. **66 Suppl 1**: p. S3-6.
3. Yang, Q., et al., *Racial differences in infant mortality attributable to birth defects in the United States, 1989-2002.* Birth Defects Res A Clin Mol Teratol, 2006. **76**(10): p. 706-13.
4. Yang, Q., M.J. Khoury, and D. Mannino, *Trends and patterns of mortality associated with birth defects and genetic diseases in the United States, 1979-1992: an analysis of multiple-cause mortality data.* Genet Epidemiol, 1997. **14**(5): p. 493-505.
5. Hoffman, T.M., et al., *Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease.* Circulation, 2003. **107**(7): p. 996-1002.
6. Parr, G.V., E.H. Blackstone, and J.W. Kirklin, *Cardiac performance and mortality early after intracardiac surgery in infants and young children.* Circulation, 1975. **51**(5): p. 867-74.
7. Wernovsky, G., et al., *Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest.* Circulation, 1995. **92**(8): p. 2226-35.
8. Wan, S., J.L. LeClerc, and J.L. Vincent, *Inflammatory response to cardiopulmonary bypass: mechanisms involved and possible therapeutic strategies.* Chest, 1997. **112**(3): p. 676-92.
9. Ando, M., et al., *Steroid supplementation: a legitimate pharmacotherapy after neonatal open heart surgery.* Ann Thorac Surg, 2005. **80**(5): p. 1672-8; discusison 1678.
10. Bronicki, R.A., et al., *Dexamethasone reduces the inflammatory response to cardiopulmonary bypass in children.* Ann Thorac Surg, 2000. **69**(5): p. 1490-5.
11. Checchia, P.A., et al., *Dexamethasone reduces postoperative troponin levels in children undergoing cardiopulmonary bypass.* Crit Care Med, 2003. **31**(6): p. 1742-5.
12. Clarizia, N.A., et al., *Improved outcomes associated with intraoperative steroid use in high-risk pediatric cardiac surgery.* Ann Thorac Surg, 2011. **91**(4): p. 1222-7.
13. Graham, E.M., et al., *Standardized preoperative corticosteroid treatment in neonates undergoing cardiac surgery: results from a randomized trial.* J Thorac Cardiovasc Surg, 2011. **142**(6): p. 1523-9.
14. Graham, E.M., et al., *Preoperative steroid treatment does not improve markers of inflammation after cardiac surgery in neonates: results from a randomized trial.* J Thorac Cardiovasc Surg, 2014. **147**(3): p. 902-8.
15. Toledo-Pereyra, L.H., et al., *Steroids in heart surgery: a clinical double-blind and randomized study.* Am Surg, 1980. **46**(3): p. 155-60.
16. Graham, E.M., *The utility of steroids in pediatric cardiac operations*.* Pediatr Crit Care Med, 2014. **15**(5): p. 492-3.
17. Pasquali, S.K., et al., *Perioperative methylprednisolone and outcome in neonates undergoing heart surgery.* Pediatrics, 2012. **129**(2): p. e385-91.

18. Garg, A.X., et al., *Steroids In caRdiac Surgery (SIRS) trial: acute kidney injury substudy protocol of an international randomised controlled trial.* BMJ Open, 2014. **4**(3): p. e004842.
19. *United States Food and Drug Administration: Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Initial Pediatric Study Plans Guidance for Industry (Draft). Accessed on-line at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf (February 1st, 2016).*
20. Scrascia, G., et al., *Perioperative steroids administration in pediatric cardiac surgery: a meta-analysis of randomized controlled trials*.* Pediatr Crit Care Med, 2014. **15**(5): p. 435-42.
21. Pasquali, S.K., et al., *Corticosteroids and outcome in children undergoing congenital heart surgery: analysis of the Pediatric Health Information Systems database.* Circulation, 2010. **122**(21): p. 2123-30.
22. Ungerleider, R.M., *Practice patterns in neonatal cardiopulmonary bypass.* ASAIO J, 2005. **51**(6): p. 813-5.
23. Felker, G.M. and A.S. Maisel, *A global rank end point for clinical trials in acute heart failure.* Circ Heart Fail, 2010. **3**(5): p. 643-6.
24. *McCullagh, P. Regression models for ordinal data (with discussion). J. R. Statist. Soc. 1980: B, 42, 109–142.*
25. Zhao, Y.D., D. Rahardja, and Y. Qu, *Sample size calculation for the Wilcoxon-Mann-Whitney test adjusting for ties.* Stat Med, 2008. **27**(3): p. 462-8.
26. Whitehead, J., *Sample size calculations for ordered categorical data.* Stat Med, 1993. **12**(24): p. 2257-71.
27. *van Elteren PH. On the combination of independent two-sample tests of Wilcoxon. Bulletin of the International Statistical Institute 1960; 37:351--361.*
28. Hauck, W.W., S. Anderson, and S.M. Marcus, *Should we adjust for covariates in nonlinear regression analyses of randomized trials?* Control Clin Trials, 1998. **19**(3): p. 249-56.
29. Pocock, S.J., et al., *The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities.* Eur Heart J, 2012. **33**(2): p. 176-82.

13 PHARMACOLOGY AND TOXICOLOGY INFORMATION

The Sponsor has not and will not conduct non-clinical studies of methylprednisolone. Information on its pharmacology and toxicology can be found in the sample product label, see Section 10.3

14 PREVIOUS HUMAN EXPERIENCE

Please refer to product label (Appendix B).

15 APPENDICES

15.1 Appendix A1: Case report form for the STS-CHSD

STS National Database
Using data to drive quality

The Society of Thoracic Surgeons
Congenital Heart Surgery Database
Data Collection Form Version 3.3
Updated January 19, 2016

ADMINISTRATIVE	
Participant ID:	Patient participating in STS-Related Clinical Trial: ☐ None ☐ Trial 1 ☐ Trial 2 ☐ Trial 3 ☐ Trial 4 ☐ Trial 5 ☐ Trial 6
	(If not None→) STS-Related Clinical Trial ID:

DEMOGRAPHICS		
Patient ID (software generated)	Patient Nat. ID (SSN):	MRN:
Last Name:	First Name:	Middle Name:
Region:	Postal Code:	Country:
Birth Location Known: ☐ Yes ☐ No		
(If Yes →) Birth City:	Birth Region:	Birth Country:
Mode of Delivery Known: ☐ Yes ☐ No *(If Yes ↓)* Mode of Delivery: ☐ Spontaneous onset labor with vaginal delivery ☐ Spontaneous onset labor with cesarean section ☐ Induction of labor with vaginal delivery ☐ Induction of labor with subsequent cesarean section ☐ Scheduled cesarean section ☐ Other cesarean section		
Mother's Gravidity and Parity known: ☐ Yes ☐ No *(If Yes ↓)* Mother's Gravidity: Mother's Parity:		
APGAR Scores Known: ☐ Yes ☐ No *(If Yes ↓)* APGAR Score at 1 minute: APGAR Score at 5 minutes:		
Mother's Name Known: ☐ Yes ☐ No		
(If Yes →) Mother's Last Name:	Mother's First Name:	Mother's Middle Name:
Mother's National ID Number (SSN) Known: ☐ Yes ☐ No ☐ Refused		
(If Yes →) Mother's National ID Number (SSN):		
DOB: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __	Birth Weight Known: ☐ Yes ☐ No	*(If Yes →)* Birth Weight (kg):
Gender: ☐ M ☐ F ☐ Ambiguous	Premature Birth: ☐ Yes ☐ No ☐ Unknown	
Gestational Age at Birth Known: ☐ Yes ☐ No	*(If Yes →)* Gestational age at birth (in weeks):	
Multiple Gestation: ☐ Yes ☐ No ☐ Unknown	Antenatal Diagnosis of Congenital Heart Disease: ☐ Yes ☐ No ☐ Unknown	
Race Documented: ☐ Yes ☐ No ☐ Patient declined to disclose *(If Yes ↓)* *(select all that apply→)* Caucasian: ☐ Yes ☐ No; Black/African American: ☐ Yes ☐ No; Asian: ☐ Yes ☐ No; Am Indian/Alaskan Native: ☐ Yes ☐ No; Native Hawaiian/Pacific Islander: ☐ Yes ☐ No; Other: ☐ Yes ☐ No		
Hispanic or Latino Ethnicity: ☐ Yes ☐ No ☐ Not Documented		
Date of Last Follow-Up: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __		
Last follow-up NYHA Classification: ☐ Not Assessed ☐ NYHA 1 ☐ NYHA 2 ☐ NYHA 3 ☐ NYHA 4		
Mortality Status at Last Follow-Up: ☐ Alive ☐ Dead *(If Dead →)*	Mortality Date: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __	

1

NONCARDIAC CONGENITAL ANATOMIC ABNORMALITIES (select all that apply)

- None
- Major abnormality of head, Choanal atresia
- Major abnormality of head, Cleft lip
- Major abnormality of head, Cleft palate
- Major abnormality of head
- Major abnormality of brain, Hydrocephalus
- Major abnormality of brain, Macrocephaly
- Major abnormality of brain, Microcephaly
- Major abnormality of brain
- Major abnormality of spinal cord, Myelomeningocele
- Major abnormality of spinal cord, Spina bifida
- Major abnormality of spinal cord
- Major abnormality of spine, Scoliosis
- Major abnormality of spine
- Major abnormality of larynx - trachea - or bronchus, Laryngomalacia
- Major abnormality of larynx - trachea - or bronchus, Congenital tracheal stenosis
- Major abnormality of larynx - trachea - or bronchus, Tracheomalacia
- Major abnormality of larynx - trachea - or bronchus, Tracheoesophageal fistula (TEF)
- Major abnormality of larynx - trachea - or bronchus, Bronchomalacia
- Major abnormality of larynx - trachea - or bronchus
- Major abnormality of lung, Congenital lobar emphysema (CLE)
- Major abnormality of lung, Cystic congenital adenomatous malformation of the lung (CAM)
- Major abnormality of lung, Cystic fibrosis
- Major abnormality of lung, Pulmonary lymphangiectasia
- Major abnormality of lung
- Major abnormality of abdominal wall, Congenital diaphragmatic hernia (CDH)
- Major abnormality of abdominal wall, Gastroschisis
- Major abnormality of abdominal wall, Omphalocele
- Major abnormality of gastrointestinal system, Biliary atresia
- Major abnormality of gastrointestinal system, Duodenal atresia
- Major abnormality of gastrointestinal system, Duodenal stenosis
- Major abnormality of gastrointestinal system, Jejunal atresia
- Major abnormality of gastrointestinal system, Jejunal stenosis
- Major abnormality of gastrointestinal system, Ileal atresia
- Major abnormality of gastrointestinal system, Ileal stenosis
- Major abnormality of gastrointestinal system, Intestinal malrotation
- Major abnormality of gastrointestinal system, Hirschsprung's disease (Congenital aganglionic megacolon)
- Major abnormality of gastrointestinal system, Stenosis of large intestine
- Major abnormality of gastrointestinal system, Atresia of large intestine
- Major abnormality of gastrointestinal system, Atresia of rectum
- Major abnormality of gastrointestinal system, Stenosis of rectum
- Major abnormality of gastrointestinal system, Anal Atresia (imperforate anus)
- Major abnormality of gastrointestinal system
- Major abnormality of kidney - ureter - or bladder
- Other

(If NCAA is Other ↓)

_____
Major Noncardiac Abnormality- Other- Specify

CHROMOSOMAL ABNORMALITIES

- ☐ No chromosomal abnormality identified
- ☐ 11p15.5
- ☐ 11q
- ☐ 12p1.21
- ☐ 12p12.1
- ☐ 12q24
- ☐ 15q21.1
- ☐ 1q42.1
- ☐ 20p12
- ☐ 22q11 deletion
- ☐ 2p21
- ☐ 3p22
- ☐ 45X0
- ☐ 47,XXY
- ☐ 4p
- ☐ 4p16
- ☐ 5p
- ☐ 6p12
- ☐ 7q11
- ☐ 7q11.23
- ☐ 7q32
- ☐ 7q34
- ☐ 8q12
- ☐ TGFBR1 or 2
- ☐ Trisomy 08
- ☐ Trisomy 09
- ☐ Trisomy 13
- ☐ Trisomy 18
- ☐ Trisomy 21
- ☐ Other chromosomal abnormality

(If ChromAb is Other chromosomal abnormality ↓)

_____
Chromosomal Abnormality - Other - Specify

SYNDROMES (select all that apply)	
☐ No syndromic abnormality identified	☐ Long QT syndrome (Ward Romano syndrome)
☐ Alagille syndrome (intrahepatic biliary duct agenesis)	☐ Marfan syndrome
☐ Apert syndrome	☐ Marfan-like syndrome
☐ Brugada syndrome (Sudden unexplained nocturnal death syndrome) (SUNDS)	☐ Mucopolysaccharidosis type IH (Hurler syndrome)
☐ Cardiofaciocutaneous syndrome	☐ Mucopolysaccharidosis type IH/S (Hurler-Scheie syndrome)
☐ Carpenter syndrome	☐ Mucopolysaccharidosis type II (Hunter syndrome)
☐ Cat-eye syndrome	☐ Mucopolysaccharidosis type IS (Scheie syndrome)
☐ CHARGE Association	☐ Noonan syndrome
☐ Cornelia de Lange syndrome	☐ Patau syndrome (Trisomy 13)
☐ Costello syndrome	☐ Pierre Robin syndrome
☐ Cri-du-chat syndrome	☐ Prune Belly syndrome
☐ Deletion 10p syndrome	☐ Rethore syndrome (Trisomy 9)
☐ Deletion 8p syndrome	☐ Fetal Rubella syndrome (Congenital rubella syndrome)
☐ DiGeorge syndrome (velocardiofacial syndrome) (conotruncal anomaly face syndrome) (22q11 deletion)	☐ Rubinstein-Taybi syndrome
☐ Down syndrome (Trisomy 21)	☐ Short QT syndrome
☐ Edwards syndrome (Trisomy 18)	☐ Sickle cell disease
☐ Ehlers- Danlos Syndrome	☐ Sickle cell trait
☐ Ellis-van Creveld syndrome	☐ Situs inversus
☐ Fetal alcohol syndrome (FAS)	☐ Smith-Lemli-Opitz syndrome
☐ Fetal drug exposure	☐ Turner syndrome (45XO)
☐ Goldenhar syndrome	☐ VACTERL syndrome (VACTER/VATER/VATERR syndrome)
☐ Heterotaxy syndrome	☐ VACTERL-H syndrome (VATER association with hydrocephalus) (Briard-Evans syndrome)
☐ Heterotaxy syndrome, Asplenia syndrome	☐ von Willebrand disease (vWD)
☐ Heterotaxy syndrome, Polysplenia syndrome	☐ Warkany syndrome (Trisomy 8)
☐ Holt-Oram syndrome	☐ Williams syndrome (Williams-Beuren syndrome)
☐ Jacobsen syndrome	☐ Wolff-Parkinson-White syndrome (WPW syndrome)
☐ Kabuki syndrome	☐ Wolf-Hirschhorn syndrome
☐ Kartagener syndrome (Siewert syndrome) (Primary ciliary dyskinesia)	☐ Other syndromic abnormality
☐ Klinefelter syndrome (XXY Syndrome)	*(If Other Syndromic abnormality, Specify ↓)*
☐ LEOPARD syndrome	
☐ Loeys-Dietz syndrome	Syndrome – Other – Specify

HOSPITALIZATION

Hospital Name: _____

Hospital Zip Code:_____ Hospital State:_____ Hospital National Provider Identifier: _____

PrimaryPayor: *(If Primary not None or missing→)*
- ☐ None/self
- ☐ Medicare
- ☐ Medicaid
- ☐ Military Health
- ☐ Indian Health Service
- ☐ Correctional Facility
- ☐ State Specific Plan
- ☐ Other Government Insurance
- ☐ Commercial Health Insurance
- ☐ Health Maintenance Organization
- ☐ Non US Plan
- ☐ Charitable Care/Foundation Funding

(If Medicare→) Primary Payor Medicare Fee for Service: ☐ Yes ☐ No

Secondary (supplemental) Payor: ☐ None/self
- ☐ Medicare
- ☐ Medicaid
- ☐ Military Health
- ☐ Indian Health Service
- ☐ Correctional Facility
- ☐ State Specific Plan
- ☐ Other Government Insurance
- ☐ Commercial Health Insurance
- ☐ Health Maintenance Organization
- ☐ Non US Plan
- ☐ Charitable Care/Foundation Funding

(If Medicare→) Secondary Payor Medicare Fee for Service: ☐ Yes ☐ No

Admission date: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __

Location From which Patient was Admitted:
☐ Home ☐ Other acute care center
☐ Other chronic care center ☐ Born at operative center

Surgery date: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __

Height (Cm): _____ Weight (Kg):_____ Age at time of surgery (in days):_____

PREOPERATIVE FACTORS (select all that apply)

- ☐ No preoperative factors identified
- ☐ Cardio-pulmonary resuscitation
- ☐ Preoperative complete AV block
- ☐ Preoperative/Preprocedural mechanical circulatory support (IABP, VAD, ECMO, or CPS)
- ☐ Shock, Persistent at time of surgery
- ☐ Shock, Resolved at time of surgery
- ☐ Diabetes mellitus, Insulin dependent
- ☐ Diabetes mellitus, Non-insulin dependent
- ☐ Hypothyroidism
- ☐ Currently taking steroids as treatment for adrenal insufficiency
- ☐ Currently taking steroids for any reason other than treatment of adrenal insufficiency
- ☐ Colostomy present
- ☐ Enterostomy of small intestine present
- ☐ Esophagostomy present
- ☐ Gastrostomy present
- ☐ Hepatic dysfunction
- ☐ Necrotizing entero-colitis, Treated medically
- ☐ Necrotizing entero-colitis, Treated surgically
- ☐ Coagulation disorder, Hypercoagulable state
- ☐ Coagulation disorder, Hypocoagulable state not secondary to medication (intrinsic hypocoagulable state)
- ☐ Coagulation disorder, Hypocoagulable state secondary to medication
- ☐ Endocarditis
- ☐ Sepsis
- ☐ Sepsis with positive blood culture
- ☐ Preoperative neurological deficit
- ☐ Seizure during lifetime
- ☐ Seizure within 48 hours prior to surgery
- ☐ Stroke, CVA, or Intracranial hemorrhage > Grade 2 during lifetime
- ☐ Stroke, CVA, or Intracranial hemorrhage > Grade 2 within 48 hours prior to surgery
- ☐ Renal dysfunction
- ☐ Renal failure requiring dialysis
- ☐ Mechanical ventilation to treat cardiorespiratory failure
- ☐ Respiratory Syncytial Virus
- ☐ Single lung
- ☐ Tracheostomy present
- ☐ Asthma
- ☐ Bronchopulmonary Dysplasia (BPD)
- ☐ ICD (AICD) ([automatic] implantable cardioverter defibrillator) present
- ☐ Pacemaker present
- ☐ Tobacco use
- ☐ Family History of Coronary Artery Disease
- ☐ Dyslipidemia
- ☐ Other preoperative factors

DIAGNOSIS			
Select **ALL** diagnosis that apply(↓)		CIRCLE the ONE PRIMARY diagnosis for this operation	Select the **ONE** FUNDAMENTAL diagnosis for this patient (↓)
Septal Defects	ASD	☐ 10=PFO	☐
		☐ 20= ASD, Secundum	☐
		☐ 30= ASD, Sinus venosus	☐
		☐ 40= ASD, Coronary sinus	☐
		☐ 50= ASD, Common atrium (single atrium)	☐
		☐ 2150= ASD, Postoperative interatrial communication	NA
	VSD	☐ 71= VSD, Type 1 (Subarterial) (Supracristal) (Conal septal defect) (Infundibular)	☐
		☐ 73= VSD, Type 2 (Perimembranous) (Paramembranous) (Conoventricular)	☐
		☐ 75= VSD, Type 3 (Inlet) (AV canal type)	☐
		☐ 77= VSD, Type 4 (Muscular)	☐
		☐ 79= VSD, Type: Gerbode type (LV-RA communication)	☐
		☐ 80= VSD, Multiple	☐
	AV Canal	☐ 100= AVC (AVSD), Complete (CAVSD)	☐
		☐ 110= AVC (AVSD), Intermediate (transitional)	☐
		☐ 120= AVC (AVSD), Partial (incomplete) (PAVSD) (ASD, primum)	☐
	AP Window	☐ 140= AP window (aortopulmonary window)	☐
		☐ 150= Pulmonary artery origin from ascending aorta (hemitruncus)	☐
	Truncus Arteriosus	☐ 160= Truncus arteriosus	☐
		☐ 170= Truncal valve insufficiency	☐
		☐ 2470= Truncal valve stenosis	NA
		☐ 2010= Truncus arteriosus + Interrupted aortic arch	☐
Pulmonary Venous Anomalies	Partial Anomalous Pulmonary Venous Connection	☐ 180= Partial anomalous pulmonary venous connection (PAPVC)	☐
		☐ 190= Partial anomalous pulmonary venous connection (PAPVC), scimitar	☐
	Total Anomalous Pulmonary Venous Connection	☐ 200=Total anomalous pulmonary venous connection (TAPVC), Type1 (supracardiac)	☐
		☐ 210=Total anomalous pulmonary venous connection (TAPVC), Type 2 (cardiac)	☐
		☐ 220=Total anomalous pulmonary venous connection (TAPVC), Type 3 (infracardiac)	☐
		☐ 230=Total anomalous pulmonary venous connection (TAPVC), Type 4 (mixed)	☐
Cor Triatriatum		☐ 250=Cor triatriatum	☐
Pulmonary Venous Stenosis		☐ 260=Pulmonary venous stenosis	☐
Systemic Venous Anomalies	Anomalous Systemic Venous Connection	☐ 270=Systemic venous anomaly	☐
	Systemic venous obstruction	☐ 280=Systemic venous obstruction	☐
Right Heart Lesions	Tetralogy of Fallot	☐ 290=TOF	☐
		☐ 2140=TOF, Pulmonary stenosis	☐
		☐ 300=TOF, AVC (AVSD)	☐
		☐ 310=TOF, Absent pulmonary valve	☐
	Pulmonary Atresia	☐ 320=Pulmonary atresia	☐
		☐ 330=Pulmonary atresia, IVS	☐
		☐ 340=Pulmonary atresia, VSD (Including TOF, PA)	☐
		☐ 350=Pulmonary atresia, VSD-MAPCA	☐
		☐ 360=MAPCA(s) (major aortopulmonary collateral[s]) (without PA-VSD)	☐
	Tricuspid Valve Disease and Ebstein's Anomaly	☐ 370=Ebstein's anomaly	☐
		☐ 380=Tricuspid regurgitation, non-Ebstein's related	☐
		☐ 390=Tricuspid stenosis	☐
		☐ 400=Tricuspid regurgitation and tricuspid stenosis	☐

		☐ 410=Tricuspid valve, Other	☐
	RVOT Obstruction and/or Pulmonary Stenosis	☐ 420=Pulmonary stenosis, Valvar	☐
		☐ 430=Pulmonary artery stenosis (hypoplasia), Main (trunk)	☐
		☐ 440=Pulmonary artery stenosis, Branch, Central (within the hilar bifurcation)	☐
		☐ 450=Pulmonary artery stenosis, Branch, Peripheral (at or beyond the hilar bifurcation)	☐
		☐ 470=Pulmonary artery, Discontinuous	☐
		☐ 490=Pulmonary stenosis, Subvalvar	☐
		☐ 500=DCRV	☐
	Pulmonary Valve Disease	☐ 510=Pulmonary valve, Other	☐
		☐ 530=Pulmonary insufficiency	☐
		☐ 540=Pulmonary insufficiency and pulmonary stenosis	☐
Shunt failure	Shunt failure	☐ 2130=Shunt Failure	NA
Conduit failure	Conduit failure	☐ 520=Conduit failure	NA
Left Heart Lesions	Aortic Valve Disease	☐ 550=Aortic stenosis, Subvalvar	☐
		☐ 560=Aortic stenosis, Valvar	☐
		☐ 570=Aortic stenosis, Supravalvar	☐
		☐ 590=Aortic valve atresia	☐
		☐ 600=Aortic insufficiency	☐
		☐ 610=Aortic insufficiency and aortic stenosis	☐
		☐ 620=Aortic valve, Other	☐
	Sinus of Valsalva Fistula/Aneurysm	☐ 630=Sinus of Valsalva aneurysm	☐
	LV to Aorta Tunnel	☐ 640=LV to aorta tunnel	☐
	Mitral Valve Disease	☐ 650=Mitral stenosis, Supravalvar mitral ring	☐
		☐ 660=Mitral stenosis, Valvar	☐
		☐ 670=Mitral stenosis, Subvalvar	☐
		☐ 680=Mitral stenosis, Subvalvar, Parachute	☐
		☐ 695=Mitral stenosis	☐
		☐ 700=Mitral regurgitation and mitral stenosis	☐
		☐ 710=Mitral regurgitation	☐
		☐ 720=Mitral valve, Other	☐
	Hypoplastic Left Heart Syndrome	☐ 730=Hypoplastic left heart syndrome (HLHS)	☐
	Shone's syndrome	☐ 2080=Shone's syndrome *{CANNOT BE PRIMARY DIAGNOSIS}*	☐
Cardiomyopathy		☐ 740=Cardiomyopathy (including dilated, restrictive, and hypertrophic)	☐
		☐ 750=Cardiomyopathy, End-stage congenital heart disease	☐
Pericardial Disease		☐ 760=Pericardial effusion	☐
		☐ 770=Pericarditis	☐
		☐ 780=Pericardial disease, Other	☐
Single Ventricle		☐ 790=Single ventricle, DILV	☐
		☐ 800=Single ventricle, DIRV	☐
		☐ 810=Single ventricle, Mitral atresia	☐
		☐ 820=Single ventricle, Tricuspid atresia	☐
		☐ 830=Single ventricle, Unbalanced AV canal	☐
		☐ 840=Single ventricle, Heterotaxia syndrome	☐
		☐ 850=Single ventricle, Other	☐
		☐ 851=Single ventricle + Total anomalous pulmonary venous connection (TAPVC)	☐
Transposition of the Great Arteries	Congenitally Corrected TGA	☐ 870=Congenitally corrected TGA	☐
		☐ 872=Congenitally corrected TGA, IVS	☐
		☐ 874=Congenitally corrected TGA, IVS-LVOTO	☐

		☐ 876=Congenitally corrected TGA, VSD	☐
		☐ 878=Congenitally corrected TGA, VSD-LVOTO	☐
	Transposition of the Great Arteries	☐ 880=TGA, IVS	☐
		☐ 890=TGA, IVS-LVOTO	☐
		☐ 900=TGA, VSD	☐
		☐ 910=TGA, VSD-LVOTO	☐
DORV		☐ 930=DORV, VSD type	☐
		☐ 940=DORV, TOF type	☐
		☐ 950=DORV, TGA type	☐
		☐ 960=DORV, Remote VSD (uncommitted VSD)	☐
		☐ 2030=DORV + AVSD (AV Canal)	☐
		☐ 975=DORV, IVS	☐
DOLV		☐ 980=DOLV	☐
Thoracic Arteries and Veins	Coarctation of Aorta and Aortic arch hypoplasia	☐ 990=Coarctation of aorta	☐
		☐ 1000=Aortic arch hypoplasia	☐
		☐ 92=VSD + Aortic arch hypoplasia	☐
		☐ 94=VSD + Coarctation of aorta	☐
	Coronary Artery Anomalies	☐ 1010=Coronary artery anomaly, Anomalous aortic origin of coronary artery (AAOCA)	☐
		☐ 1020=Coronary artery anomaly, Anomalous pulmonary origin (includes ALCAPA)	☐
		☐ 1030=Coronary artery anomaly, Fistula	☐
		☐ 1040=Coronary artery anomaly, Aneurysm	☐
		☐ 2420=Coronary artery anomaly, Ostial atresia	☐
		☐ 1050=Coronary artery anomaly, Other	☐
	Interrupted Arch	☐ 1070=Interrupted aortic arch	☐
		☐ 2020=Interrupted aortic arch + VSD	☐
		☐ 2000=Interrupted aortic arch + AP window (aortopulmonary window)	☐
	Patent Ductus Arteriosus	☐ 1080=Patent ductus arteriosus	☐
	Vascular rings and Slings	☐ 1090=Vascular ring	☐
		☐ 1100=Pulmonary artery sling	☐
	Aortic Aneurysm	☐ 1110=Aortic aneurysm (including pseudoaneurysm)	☐
	Aortic Dissection	☐ 1120=Aortic dissection	☐
Thoracic and Mediastinal Disease	Lung Disease	☐ 1130=Lung disease, Benign	☐
		☐ 1140=Lung disease, Malignant	☐
	Tracheal	☐ 1160=Tracheal stenosis	☐
		☐ 2430=Tracheomalacia	☐
		☐ 1170=Airway disease	☐
	Pleural Disease	☐ 1430=Pleural disease, Benign	☐
		☐ 1440=Pleural disease, Malignant	☐
		☐ 1450=Pneumothorax	☐
		☐ 1460=Pleural effusion	☐
		☐ 1470=Chylothorax	☐
		☐ 1480=Empyema	☐
	Esophageal Disease	☐ 1490=Esophageal disease, Benign	☐
		☐ 1500=Esophageal disease, Malignant	☐
	Mediastinal Disease	☐ 1505=Mediastinal disease	☐
		☐ 1510=Mediastinal disease, Benign	☐
		☐ 1520=Mediastinal disease, Malignant	☐

	Diaphragmatic Disease	☐ 1540=Diaphragm paralysis	☐
		☐ 1550=Diaphragm disease, Other	☐
	Chest Wall	☐ 2160=Rib tumor, Benign	☐
		☐ 2170=Rib tumor, Malignant	☐
		☐ 2180=Rib tumor, Metastatic	☐
		☐ 2190=Sternal tumor, Benign	☐
		☐ 2200=Sternal tumor, Malignant	☐
		☐ 2210=Sternal tumor, Metastatic	☐
	Pectus Excavatum, Carinatum	☐ 2220=Pectus carinatum	☐
		☐ 2230=Pectus excavatum	☐
	Thoracic Outlet	☐ 2240=Thoracic outlet syndrome	☐
Electrophysiological		☐ 1180=Arrhythmia	☐
		☐ 2440=Arrhythmia, Atrial, Atrial fibrillation	☐
		☐ 2450=Arrhythmia, Atrial, Atrial flutter	☐
		☐ 2460=Arrhythmia, Atrial, Other	☐
		☐ 2050=Arrhythmia, Junctional	☐
		☐ 2060=Arrhythmia, Ventricular	☐
		☐ 1185=Arrhythmia, Heart block	☐
		☐ 1190=Arrhythmia, Heart block, Acquired	☐
		☐ 1200=Arrhythmia, Heart block, Congenital	☐
		☐ 1220=Arrhythmia, Pacemaker, Indication for replacement	NA
Miscellaneous, Other		☐ 1230=Atrial Isomerism, Left *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 1240=Atrial Isomerism, Right *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 2090=Dextrocardia *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 2100=Levocardia *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 2110=Mesocardia *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 2120=Situs inversus *{CANNOT BE PRIMARY DIAGNOSIS}*	NA
		☐ 1250=Aneurysm, Ventricular, Right (including pseudoaneurysm)	☐
		☐ 1260=Aneurysm, Ventricular, Left (including pseudoaneurysm)	☐
		☐ 1270=Aneurysm, Pulmonary artery	☐
		☐ 1280=Aneurysm, Other	☐
		☐ 1290=Hypoplastic RV	☐
		☐ 1300=Hypoplastic LV	☐
		☐ 2070=Postoperative bleeding	NA
		☐ 1310=Mediastinitis	☐
		☐ 1320=Endocarditis	☐
		☐ 1325=Rheumatic heart disease *{CANNOT BE PRIMARY DIAGNOSIS}*	☐
		☐ 1330=Prosthetic valve failure	NA
		☐ 1340=Myocardial infarction	☐
		☐ 1350=Cardiac tumor	☐
		☐ 1360=Pulmonary AV fistula	☐
		☐ 1370=Pulmonary embolism	☐
		☐ 1385=Pulmonary vascular obstructive disease	☐
		☐ 1390=Pulmonary vascular obstructive disease (Eisenmenger's)	☐
		☐ 1400=Primary pulmonary hypertension	☐
		☐ 1410=Persistent fetal circulation	☐
		☐ 1420=Meconium aspiration	☐

		☐ 2250=Kawasaki Disease	☐
		☐ 1560=Cardiac, Other	☐
		☐ 1570=Thoracic and/or mediastinal, Other	☐
		☐ 1580=Peripheral vascular, Other	☐
		☐ 2260=Complication of cardiovascular catheterization procedure	NA
		☐ 2270=Complication of cardiovascular catheterization procedure, Device embolization	NA
		☐ 2280=Complication of cardiovascular catheterization procedure, Device malfunction	NA
		☐ 2290=Complication of cardiovascular catheterization procedure, Perforation	NA
		☐ 2300=Complication of interventional radiology procedure	NA
		☐ 2310=Complication of interventional radiology procedure, Device embolization	NA
		☐ 2320=Complication of interventional radiology procedure, Device malfunction	NA
		☐ 2330=Complication of interventional radiology procedure, Perforation	NA
		☐ 2340=Foreign body, Intracardiac foreign body	NA
		☐ 2350=Foreign body, Intravascular foreign body	NA
		☐ 2360=Open sternum with closed skin	NA
		☐ 2370=Open sternum with open skin (includes membrane placed to close skin)	NA
		☐ 2380=Retained sternal wire causing irritation	NA
		☐ 2390=Syncope	NA
		☐ 2400=Trauma, Blunt	☐
		☐ 2410=Trauma, Penetrating	☐
		☐ 7000=Normal heart	☐
		☐ 7777=Miscellaneous, Other	☐
STATUS POST (No "Status post – diagnoses" can be a primary diagnosis or fundamental diagnosis)			
Septal Defects	ASD	☐ 4010=Status post - PFO, Primary closure	
		☐ 4020=Status post - ASD repair, Primary closure	
		☐ 4030=Status post - ASD repair, Patch	
		☐ 4040=Status post - ASD repair, Device	
		☐ 6110=Status post - ASD repair, Patch + PAPVC repair	
		☐ 4050=Status post - ASD, Common atrium (single atrium), Septation	
		☐ 4060=Status post - ASD creation/enlargement	
		☐ 4070=Status post - ASD partial closure	
		☐ 4080=Status post - Atrial septal fenestration	
		☐ 4085=Status post - Atrial fenestration closure	
	VSD	☐ 4100=Status post - VSD repair, Primary closure	
		☐ 4110=Status post - VSD repair, Patch	
		☐ 4120=Status post - VSD repair, Device	
		☐ 4130=Status post - VSD, Multiple, Repair	
		☐ 4140=Status post - VSD creation/enlargement	
		☐ 4150=Status post - Ventricular septal fenestration	
	AV Canal	☐ 4170=Status post - AVC (AVSD) repair, Complete (CAVSD)	
		☐ 4180=Status post - AVC (AVSD) repair, Intermediate (Transitional)	
		☐ 4190=Status post - AVC (AVSD) repair, Partial (Incomplete) (PAVSD)	
		☐ 6300=Status post - Valvuloplasty, Common atrioventricular valve	
		☐ 6250=Status post - Valvuloplasty converted to valve replacement in the same operation, Common atrioventricular valve	
		☐ 6230=Status post - Valve replacement, Common atrioventricular valve	
	AP Window	☐ 4210=Status post - AP window repair	
		☐ 4220=Status post - Pulmonary artery origin from ascending aorta (hemitruncus) repair	
	Truncus Arteriosus	☐ 4230=Status post - Truncus arteriosus repair	

		☐ 4240=Status post - Valvuloplasty, Truncal valve ☐ 6290=Status post - Valvuloplasty converted to valve replacement in the same operation, Truncal valve ☐ 4250=Status post - Valve replacement, Truncal valve ☐ 6220=Status post - Truncus + Interrupted aortic arch repair (IAA) repair
Pulmonary Venous Anomalies	Partial Anomalous Pulmonary Venous Connection	☐ 4260=Status post - PAPVC repair ☐ 4270=Status post - PAPVC, Scimitar, Repair ☐ 6120=Status post - PAPVC repair, Baffle redirection to left atrium with systemic vein translocation (Warden) (SVC sewn to right atrial appendage)
	Total Anomalous Pulmonary Venous Connection	☐ 4280=Status post - TAPVC repair ☐ 6200=Status post - TAPVC repair + Shunt - systemic-to-pulmonary
Cor Triatriatum		☐ 4290=Status post - Cor triatriatum repair
Pulmonary Venous Stenosis		☐ 4300=Status post - Pulmonary venous stenosis repair
Systemic Venous Anomalies	Anomalous Systemic Venous Connection	☐ 4310=Status post - Atrial baffle procedure (non-Mustard, non-Senning) ☐ 4330=Status post - Anomalous systemic venous connection repair
	Systemic venous obstruction	☐ 4340=Status post - Systemic venous stenosis repair
Right Heart Lesions	Tetralogy of Fallot	☐ 4350=Status post - TOF repair, No ventriculotomy ☐ 4360=Status post - TOF repair, Ventriculotomy, Nontransanular patch ☐ 4370=Status post - TOF repair, Ventriculotomy, Transanular patch ☐ 4380=Status post - TOF repair, RV-PA conduit ☐ 4390=Status post - TOF - AVC (AVSD) repair ☐ 4400=Status post - TOF - Absent pulmonary valve repair
	Pulmonary Atresia/VSD	☐ 4420=Status post - Pulmonary atresia - VSD (including TOF, PA) repair ☐ 6700=Status post - Pulmonary atresia - VSD - MAPCA repair, Complete single stage repair (1-stage that includes bilateral pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit]) ☐ 6710=Status post - Pulmonary atresia - VSD - MAPCA repair, Status post prior complete unifocalization (includes VSD closure + RV to PA connection [with or without conduit]) ☐ 6720=Status post - Pulmonary atresia - VSD - MAPCA repair, Status post prior incomplete unifocalizarion (includes completion of pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit]) ☐ 6730=Status post - Unifocalization MAPCA(s), Bilateral pulmonary unifocalization - Complete unifocalization (all usable MAPCA[s] are incorporated) ☐ 6740=Status post - Unifocalization MAPCA(s), Bilateral pulmonary unifocalization - Incomplete unifocalization (not all usable MAPCA[s] are incorporated) ☐ 6750=Status post - Unifocalization MAPCA(s), Unilateral pulmonary unifocalization ☐ 4440=Status post – Unifocalization MAPCA(s) ☐ 4450=Status post - Occlusion of MAPCA(s)
	Tricuspid Valve Disease and Ebstein's Anomaly	☐ 4460=Status post - Valvuloplasty, Tricuspid ☐ 6280=Status post - Valvuloplasty converted to valve replacement in the same operation, Tricuspid ☐ 4465=Status post - Ebstein's repair ☐ 4470=Status post - Valve replacement, Tricuspid (TVR) ☐ 4480=Status post - Valve closure, Tricuspid (exclusion, univentricular approach) ☐ 4490=Status post - Valve excision, Tricuspid (without replacement) ☐ 4500=Status post - Valve surgery, Other, Tricuspid
	RVOT Obstruction, IVS Pulmonary Stenosis	☐ 4510=Status post - RVOT procedure ☐ 4520=Status post - 1 1/2 ventricular repair ☐ 4530=Status post - PA, reconstruction (plasty), Main (trunk) ☐ 4540=Status post - PA, reconstruction (plasty), Branch, Central (within the hilar bifurcation) ☐ 4550=Status post - PA, reconstruction (plasty), Branch, Peripheral (at or beyond the hilar bifurcation)

		☐ 4570=Status post - DCRV repair
	Pulmonary Valve Disease	☐ 4590=Status post - Valvuloplasty, Pulmonic ☐ 6270=Status post - Valvuloplasty converted to valve replacement in the same operation, Pulmonic ☐ 4600=Status post - Valve replacement, Pulmonic (PVR) ☐ 4630=Status post - Valve excision, Pulmonary (without replacement) ☐ 4640=Status post - Valve closure, Semilunar ☐ 4650=Status post - Valve surgery, Other, Pulmonic
Conduit operations	Conduit operations	☐ 4610=Status post - Conduit placement, RV to PA ☐ 4620=Status post - Conduit placement, LV to PA ☐ 5774=Status post - Conduit placement, Ventricle to aorta ☐ 5772=Status post - Conduit placement, Other
	Conduit Stenosis / Insufficiency	☐ 4580=Status post - Conduit reoperation
Left Heart Lesions	Aortic Valve Disease	☐ 4660=Status post - Valvuloplasty, Aortic ☐ 6240=Status post - Valvuloplasty converted to valve replacement in the same operation, Aortic ☐ 6310=Status post - Valvuloplasty converted to valve replacement in the same operation, Aortic – with Ross procedure ☐ 6320=Status post - Valvuloplasty converted to valve replacement in the same operation, Aortic – with Ross-Konno procedure ☐ 4670=Status post - Valve replacement, Aortic (AVR) ☐ 4680=Status post - Valve replacement, Aortic (AVR), Mechanical ☐ 4690=Status post - Valve replacement, Aortic (AVR), Bioprosthetic ☐ 4700=Status post - Valve replacement, Aortic (AVR), Homograft ☐ 4715=Status post - Aortic root replacement, Bioprosthetic ☐ 4720=Status post - Aortic root replacement, Mechanical ☐ 4730=Status post - Aortic root replacement, Homograft ☐ 4735=Status post - Aortic root replacement, Valve sparing ☐ 4740=Status post - Ross procedure ☐ 4750=Status post - Konno procedure ☐ 4760=Status post - Ross-Konno procedure ☐ 4770=Status post - Other annular enlargement procedure ☐ 4780=Status post - Aortic stenosis, Subvalvar, Repair ☐ 6100=Status post - Aortic stenosis, Subvalvar, Repair, With myectomy for IHSS ☐ 4790=Status post - Aortic stenosis, Supravalvar, Repair ☐ 4800=Status post - Valve surgery, Other, Aortic
	Sinus of Valsalva Aneurysm	☐ 4810=Status post - Sinus of Valsalva, Aneurysm repair
	LV to Aorta Tunnel	☐ 4820=Status post - LV to aorta tunnel repair
	Mitral Valve Disease	☐ 4830=Status post - Valvuloplasty, Mitral ☐ 6260=Status post - Valvuloplasty converted to valve replacement in the same operation, Mitral ☐ 4840=Status post - Mitral stenosis, Supravalvar mitral ring repair ☐ 4850=Status post - Valve replacement, Mitral (MVR) ☐ 4860=Status post - Valve surgery, Other, Mitral
	Hypoplastic Left Heart and Related malformations	☐ 4870=Status post - Norwood procedure ☐ 4880=Status post - HLHS biventricular repair ☐ 6755=Status post - Conduit insertion right ventricle to pulmonary artery + Intraventricular tunnel left ventricle to neoaorta + arch reconstruction (Rastelli and Norwood type arch reconstruction) (Yasui)
Hybrid		☐ 6160=Status post - Hybrid Approach "Stage 1", Application of RPA & LPA bands ☐ 6170=Status post - Hybrid Approach "Stage 1", Stent placement in arterial duct (PDA)

		☐ 6180=Status post - Hybrid Approach "Stage 1", Stent placement in arterial duct (PDA) + application of RPA & LPA bands ☐ 6140=Status post - Hybrid approach "Stage 2", Aortopulmonary amalgamation + Superior Cavopulmonary anastomosis(es) + PA Debanding + Aortic arch repair (Norwood [Stage 1] + Superior Cavopulmonary anastomosis(es) + PA Debanding) ☐ 6150=Status post - Hybrid approach "Stage 2", Aortopulmonary amalgamation + Superior Cavopulmonary anastomosis(es) + PA Debanding + Without aortic arch repair ☐ 6760=Status post – Hybrid Approach, Transcardiac balloon dilatation ☐ 6770=Status post – Hybrid Approach, Transcardiac transcatheter device placement
Cardiomyopathy		☐ 1590=Status post - Transplant, Heart ☐ 1610=Status post - Transplant, Heart and lung ☐ 4910=Status post - Partial left ventriculectomy (LV volume reduction surgery) (Batista)
Pericardial Disease		☐ 4920=Status post - Pericardial drainage procedure ☐ 4930=Status post - Pericardiectomy ☐ 4940=Status post - Pericardial procedure, Other
Single Ventricle		☐ 4950=Status post - Fontan, Atrio-pulmonary connection ☐ 4960=Status post - Fontan, Atrio-ventricular connection ☐ 4970=Status post - Fontan, TCPC, Lateral tunnel, Fenestrated ☐ 4980=Status post - Fontan, TCPC, Lateral tunnel, Nonfenestrated ☐ 5000=Status post - Fontan, TCPC, External conduit, Fenestrated ☐ 5010=Status post - Fontan, TCPC, External conduit, Nonfenestrated ☐ 6780=Status post - Fontan, TCPC, Intra/extracardiac conduit, Fenestrated ☐ 6790=Status post - Fontan, TCPC, Intra/extracardiac conduit, Nonfenestrated ☐ 7310=Status post - Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Fenestrated ☐ 7320=Status post - Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Nonfenestrated ☐ 5025=Status post - Fontan revision or conversion (Re-do Fontan) ☐ 5030=Status post - Fontan, Other ☐ 6340=Status post - Fontan + Atrioventricular valvuloplasty ☐ 5035=Status post - Ventricular septation
Transposition of the Great Arteries	Congenitally Corrected TGA	☐ 5050=Status post - Congenitally corrected TGA repair, Atrial switch and ASO (double switch) ☐ 5060=Status post - Congenitally corrected TGA repair, Atrial switch and Rastelli ☐ 5070=Status post - Congenitally corrected TGA repair, VSD closure ☐ 5080=Status post - Congenitally corrected TGA repair, VSD closure and LV to PA conduit ☐ 5090=Status post - Congenitally corrected TGA repair, Other
	Transposition of the Great Arteries	☐ 5110=Status post - Arterial switch operation (ASO) ☐ 5120=Status post - Arterial switch operation (ASO) and VSD repair ☐ 5123=Status post - Arterial switch procedure + Aortic arch repair ☐ 5125=Status post - Arterial switch procedure and VSD repair + Aortic arch repair ☐ 5130=Status post - Senning ☐ 5140=Status post - Mustard ☐ 5145=Status post - Atrial baffle procedure, Mustard or Senning revision ☐ 5150=Status post - Rastelli ☐ 5160=Status post - REV ☐ 6190=Status post - Aortic root translocation over left ventricle (Including Nikaidoh procedure) ☐ 6210=Status post - TGA, Other procedures (Kawashima, LV-PA conduit, other)
DORV		☐ 5180=Status post - DORV, Intraventricular tunnel repair
DOLV		☐ 5200=Status post - DOLV repair
Thoracic Arteries and Veins		☐ 5210=Status post - Coarctation repair, End to end ☐ 5220=Status post - Coarctation repair, End to end, Extended

	Coarctation of Aorta and Aortic arch hypoplasia	☐ 5230=Status post - Coarctation repair, Subclavian flap ☐ 5240=Status post - Coarctation repair, Patch aortoplasty ☐ 5250=Status post - Coarctation repair, Interposition graft ☐ 5260=Status post - Coarctation repair, Other ☐ 5275=Status post - Coarctation repair + VSD repair ☐ 5280=Status post - Aortic arch repair ☐ 5285=Status post - Aortic arch repair + VSD repair
	Coronary Artery Anomalies	☐ 5290=Status post - Coronary artery fistula ligation ☐ 5291=Status post - Anomalous origin of coronary artery from pulmonary artery repair ☐ 5300=Status post - Coronary artery bypass ☐ 5305=Status post - Anomalous aortic origin of coronary artery (AAOCA) repair ☐ 5310=Status post - Coronary artery procedure, Other
	Interrupted Arch	☐ 5320=Status post - Interrupted aortic arch repair
	Patent Ductus Arteriosus	☐ 5330=Status post - PDA closure, Surgical ☐ 5340=Status post - PDA closure, Device
	Vascular Rings and Slings	☐ 5360=Status post - Vascular ring repair ☐ 5365=Status post - Aortopexy ☐ 5370=Status post - Pulmonary artery sling repair
	Aortic Aneurysm	☐ 5380=Status post - Aortic aneurysm repair
	Aortic Dissection	☐ 5390=Status post - Aortic dissection repair
Thoracic and Mediastinal Disease	Lung Disease	☐ 5400=Status post - Lung biopsy ☐ 1600=Status post - Transplant, lung(s) ☐ 5420=Status post - Lung procedure, Other
	Tracheal Stenosis	☐ 5440=Status post - Tracheal procedure
	Chest Wall	☐ 6800=Status post - Muscle flap, Trunk (i.e. intercostal, pectus, or serratus muscle) ☐ 6810=Status post - Muscle flap, Trunk (i.e. latissimus dorsi) ☐ 6820=Status post - Removal, Sternal wire ☐ 6830=Status post - Rib excision, Complete ☐ 6840=Status post - Rib excision, Partial ☐ 6850=Status post - Sternal fracture, Open treatment ☐ 6860=Status post - Sternal resection, Radical resection of the sternum ☐ 6870=Status post - Sternal resection, Radical resection of the sternum with mediastinal lymphadenectomy ☐ 6880=Status post - Tumor of chest wall, Excision including ribs ☐ 6890=Status post - Tumor of chest wall, Excision including ribs, With reconstruction ☐ 6900=Status post - Tumor of soft tissue of thorax, Excision of deep subfascial or intramuscular tumor ☐ 6910=Status post - Tumor of soft tissue of thorax, Excision of subcutaneous tumor ☐ 6920=Status post - Tumor of soft tissue of thorax, Radical resection
	Neck	☐ 6930=Status post - Hyoid myotomy and suspension ☐ 6940=Status post - Muscle flap, Neck ☐ 6950=Status post - Procedure on neck ☐ 6960=Status post - Tumor of soft tissue of neck, Excision of deep subfascial or intramuscular tumor ☐ 6970=Status post - Tumor of soft tissue of neck, Excision of subcutaneous tumor ☐ 6980=Status post - Tumor of soft tissue of neck, Radical resection
	Pectus Excavatum, Carinatum	☐ 6990=Status post - Pectus bar removal ☐ 7005=Status post - Pectus bar repositioning ☐ 7010=Status post - Pectus repair, Minimally invasive repair (Nuss), With thoracoscopy ☐ 7020=Status post - Pectus repair, Minimally invasive repair (Nuss), Without thoracoscopy ☐ 7030=Status post - Pectus repair, Open repair
	Thoracic Outlet	☐ 7040=Status post - Division of scalenus anticus, With resection of a cervical rib

		☐ 7050=Status post - Division of scalenus anticus, Without resection of a cervical rib ☐ 7060=Status post - Rib excision, Excision of a cervical rib ☐ 7070=Status post - Rib excision, Excision of a cervical rib, With sympathectomy ☐ 7080=Status post - Rib excision, Excision of first rib ☐ 7090=Status post - Rib excision, Excision of first rib, With sympathectomy
	Thorax	☐ 7100=Status post - Procedure on thorax
Electrophysiological		☐ 5450=Status post - Pacemaker implantation, Permanent ☐ 5460=Status post - Pacemaker procedure ☐ 6350=Status post - Explantation of pacing system ☐ 5470=Status post - ICD (AICD) implantation ☐ 5480=Status post - ICD (AICD) ([automatic] implantable cardioverter defibrillator) procedure ☐ 5490=Status post - Arrhythmia surgery - atrial, Surgical Ablation ☐ 5500=Status post - Arrhythmia surgery - ventricular, Surgical Ablation
Interventional Cardiology Procedures		☐ 6500=Status post - Cardiovascular catheterization procedure, Diagnostic ☐ 6520=Status post - Cardiovascular catheterization procedure, Diagnostic, Angiographic data obtained ☐ 6550=Status post - Cardiovascular catheterization procedure, Diagnostic, Electrophysiology alteration ☐ 6540=Status post - Cardiovascular catheterization procedure, Diagnostic, Hemodynamic alteration ☐ 6510=Status post - Cardiovascular catheterization procedure, Diagnostic, Hemodynamic data obtained ☐ 6530=Status post - Cardiovascular catheterization procedure, Diagnostic, Transluminal test occlusion ☐ 6410=Status post - Cardiovascular catheterization procedure, Therapeutic ☐ 6670=Status post - Cardiovascular catheterization procedure, Therapeutic, Adjunctive therapy ☐ 6570=Status post - Cardiovascular catheterization procedure, Therapeutic, Balloon dilation ☐ 6590=Status post - Cardiovascular catheterization procedure, Therapeutic, Balloon valvotomy ☐ 6600=Status post - Cardiovascular catheterization procedure, Therapeutic, Coil implantation ☐ 6610=Status post - Cardiovascular catheterization procedure, Therapeutic, Device implantation ☐ 7110=Status post - Cardiovascular catheterization procedure, Therapeutic, Device implantation attempted ☐ 6690=Status post - Cardiovascular catheterization procedure, Therapeutic, Electrophysiological ablation ☐ 7120=Status post - Cardiovascular catheterization procedure, Therapeutic, Intravascular foreign body removal ☐ 6640=Status post - Cardiovascular catheterization procedure, Therapeutic, Perforation (establishing interchamber and/or intervessel communication) ☐ 6580=Status post - Cardiovascular catheterization procedure, Therapeutic, Septostomy ☐ 6620=Status post - Cardiovascular catheterization procedure, Therapeutic, Stent insertion ☐ 6630=Status post - Cardiovascular catheterization procedure, Therapeutic, Stent re-dilation ☐ 6650=Status post - Cardiovascular catheterization procedure, Therapeutic, Transcatheter Fontan completion ☐ 6660=Status post - Cardiovascular catheterization procedure, Therapeutic, Transcatheter implantation of valve
Palliative Procedures		☐ 5590=Status post - Shunt, Systemic to pulmonary, Modified Blalock-Taussig Shunt (MBTS) ☐ 5600=Status post - Shunt, Systemic to pulmonary, Central (shunt from aorta) ☐ 7130=Status post - Shunt, Systemic to pulmonary, Central (shunt from aorta) Central shunt with an end-to-side connection between the transected main pulmonary artery and the side of the ascending aorta (i.e. Mee shunt) ☐ 7230=Status post – Shunt, Systemic to pulmonary, Potts – Smith type (descending aorta to pulmonary artery) ☐ 5610=Status post - Shunt, Systemic to pulmonary, Other ☐ 5630=Status post - Shunt, Ligation and takedown ☐ 6095=Status post - Shunt, Reoperation ☐ 5640=Status post - PA banding (PAB) ☐ 5650=Status post - PA debanding

	☐ 7200=Status post - PA band adjustment ☐ 5660=Status post - Damus-Kaye-Stansel procedure (DKS) (creation of AP anastomosis without arch reconstruction) ☐ 5670=Status post - Bidirectional cavopulmonary anastomosis (BDCPA) (bidirectional Glenn) ☐ 5680=Status post - Glenn (unidirectional cavopulmonary anastomosis) (unidirectional Glenn) ☐ 5690=Status post - Bilateral bidirectional cavopulmonary anastomosis (BBDCPA) (bilateral bidirectional Glenn) ☐ 5700=Status post - HemiFontan ☐ 6330=Status post - Superior cavopulmonary anastomosis(es) (Glenn or HemiFontan) + Atrioventricular valvuloplasty ☐ 6130=Status post - Superior Cavopulmonary anastomosis(es) + PA reconstruction ☐ 7300=Status post - Takedown of superior cavopulmonary anastomosis ☐ 7140=Status post - Hepatic vein to azygous vein connection, Direct ☐ 7150=Status post - Hepatic vein to azygous vein connection, Interposition graft ☐ 7160=Status post - Kawashima operation (superior cavopulmonary connection in setting of interrupted IVC with azygous continuation) ☐ 5710=Status post - Palliation, Other
Fetal Interventions	☐ 7240=Status post – Attempted fetal intervention, percutaneous transcatheter directed at interatrial septum ☐ 7250=Status post – Attempted fetal intervention, percutaneous transcatheter directed at aortic valve ☐ 7260=Status post – Attempted fetal intervention, percutaneous transcatheter directed at pulmonic valve ☐ 7270=Status post – Attempted fetal intervention “open” (maternal laparotomy with hysterotomy), directed at interatrial septum ☐ 7280=Status post – Attempted fetal intervention “open” (maternal laparotomy with hysterotomy), directed at aortic valve ☐ 7290=Status post – Attempted fetal intervention “open” (maternal laparotomy with hysterotomy), directed at pulmonic valve
Mechanical Support	☐ 6360=Status post - ECMO cannulation ☐ 6370=Status post - ECMO decannulation ☐ 5910=Status post - ECMO procedure ☐ 5900=Status post - Intraaortic balloon pump (IABP) insertion ☐ 5920=Status post - Right/left heart assist device procedure ☐ 6390=Status post - VAD explantation ☐ 6380=Status post - VAD implantation ☐ 7170=Status post - VAD change out
Anesthetic procedures	☐ 6420=Status post - Echocardiography procedure, Sedated transesophageal echocardiogram ☐ 6430=Status post - Echocardiography procedure, Sedated transthoracic echocardiogram ☐ 6435=Status post - Non-cardiovascular, Non-thoracic procedure on cardiac patient with cardiac anesthesia ☐ 6440=Status post - Radiology procedure on cardiac patient, Cardiac Computerized Axial Tomography (CT Scan) ☐ 6450=Status post - Radiology procedure on cardiac patient, Cardiac Magnetic Resonance Imaging (MRI) ☐ 6460=Status post - Radiology procedure on cardiac patient, Diagnostic radiology ☐ 6470=Status post - Radiology procedure on cardiac patient, Non-Cardiac Computerized Tomography (CT) on cardiac patient ☐ 6480=Status post - Radiology procedure on cardiac patient, Non-cardiac Magnetic Resonance Imaging (MRI) on cardiac patient ☐ 6490=Status post - Radiology procedure on cardiac patient, Therapeutic radiology

Miscellaneous Procedures	☐ 5720=Status post - Aneurysm, Ventricular, Right, Repair ☐ 5730=Status post - Aneurysm, Ventricular, Left, Repair ☐ 5740=Status post - Aneurysm, Pulmonary artery, Repair ☐ 5760=Status post - Cardiac tumor resection ☐ 5780=Status post - Pulmonary AV fistula repair/occlusion ☐ 5790=Status post - Ligation, Pulmonary artery

	☐ 5802=Status post - Pulmonary embolectomy, Acute pulmonary embolus ☐ 5804=Status post - Pulmonary embolectomy, Chronic pulmonary embolus ☐ 5810=Status post - Pleural drainage procedure ☐ 5820=Status post - Pleural procedure, Other ☐ 5830=Status post - Ligation, Thoracic duct ☐ 5840=Status post - Decortication ☐ 5850=Status post - Esophageal procedure ☐ 5860=Status post - Mediastinal procedure ☐ 5870=Status post - Bronchoscopy ☐ 5880=Status post - Diaphragm plication ☐ 5890=Status post - Diaphragm procedure, Other ☐ 5930=Status post - VATS (video-assisted thoracoscopic surgery) ☐ 5940=Status post - Minimally invasive procedure ☐ 5950=Status post - Bypass for noncardiac lesion ☐ 5960=Status post - Delayed sternal closure ☐ 5970=Status post - Mediastinal exploration ☐ 5980=Status post - Sternotomy wound drainage ☐ 7180=Status post - Intravascular stent removal ☐ 7220= Status post – Removal of transcatheter delivered device from heart ☐ 7210= Status post – Removal of transcatheter delivered device from blood vessel ☐ 5990=Status post - Thoracotomy, Other ☐ 6000=Status post - Cardiotomy, Other ☐ 6010=Status post - Cardiac procedure, Other ☐ 6020=Status post - Thoracic and/or mediastinal procedure, Other ☐ 6030=Status post - Peripheral vascular procedure, Other ☐ 6040=Status post - Miscellaneous procedure, Other ☐ 11777=Status post - Other procedure

PROCEDURES		
Select **ALL** procedures that apply. (↓)		Circle the **ONE** PRIMARY procedure for this operation.
Septal Defects	ASD	☐ 10= PFO, Primary closure ☐ 20= ASD repair, Primary closure ☐ 30= ASD repair, Patch ☐ 40= ASD repair, Device ☐ 2110= ASD repair, Patch + PAPVC repair ☐ 50= ASD, Common atrium (single atrium), Septation ☐ 60= ASD creation/enlargement ☐ 70= ASD partial closure ☐ 80= Atrial septal fenestration ☐ 85= Atrial fenestration closure
	VSD	☐ 100= VSD repair, Primary closure ☐ 110= VSD repair, Patch ☐ 120= VSD repair, Device ☐ 130= VSD, Multiple, Repair ☐ 140= VSD creation/enlargement ☐ 150= Ventricular septal fenestration
	AV Canal	☐ 170= AVC (AVSD) repair, Complete (CAVSD) ☐ 180= AVC (AVSD) repair, Intermediate (Transitional) ☐ 190= AVC (AVSD) repair, Partial (Incomplete) (PAVSD) ☐ 2300= Valvuloplasty, Common atrioventricular valve

		☐ 2250= Valvuloplasty converted to valve replacement in the same operation, Common atrioventricular valve ☐ 2230= Valve replacement, Common atrioventricular valve
	AP Window	☐ 210= AP window repair ☐ 220= Pulmonary artery origin from ascending aorta (hemitruncus) repair
	Truncus Arteriosus	☐ 230= Truncus arteriosus repair ☐ 240= Valvuloplasty, Truncal valve ☐ 2290= Valvuloplasty converted to valve replacement in the same operation, Truncal valve ☐ 250= Valve replacement, Truncal valve ☐ 2220= Truncus + Interrupted aortic arch repair (IAA) repair
Pulmonary Venous Anomalies	Partial Anomalous Pulmonary Venous Connection	☐ 260= PAPVC repair ☐ 270= PAPVC, Scimitar, Repair ☐ 2120= PAPVC repair, Baffle redirection to left atrium with systemic vein translocation (Warden) (SVC sewn to right atrial appendage)
	Total Anomalous Pulmonary Venous Connection	☐ 280= TAPVC repair ☐ 2200= TAPVC repair + Shunt - systemic-to-pulmonary
Cor Triatriatum		☐ 290= Cor triatriatum repair
Pulmonary Venous Stenosis		☐ 300= Pulmonary venous stenosis repair
Systemic Venous Anomalies	Anomalous Systemic Venous Connection	☐ 310= Atrial baffle procedure (non-Mustard, non-Senning) ☐ 330= Anomalous systemic venous connection repair
	Systemic venous obstruction	☐ 340= Systemic venous stenosis repair
Right Heart Lesions	Tetralogy of Fallot	☐ 350= TOF repair, No Ventriculotomy ☐ 360= TOF repair, Ventriculotomy, Nontransanular patch ☐ 370= TOF repair, Ventriculotomy, Transanular patch ☐ 380= TOF repair, RV-PA conduit ☐ 390= TOF - AVC (AVSD) repair ☐ 400= TOF - Absent pulmonary valve repair
	Pulmonary Atresia/VSD	☐ 420= Pulmonary atresia - VSD (including TOF, PA) repair ☐ 2700= Pulmonary atresia - VSD – MAPCA repair, Complete single stage repair (1 stage that includes bilateral pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit]) ☐ 2710= Pulmonary atresia - VSD – MAPCA repair, Status post prior complete unifocalization (includes VSD closure + RV to PA connection [with or without conduit]) ☐ 2720= Pulmonary atresia - VSD – MAPCA repair, Status post prior incomplete unifocalization (includes completion of pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit]) ☐ 2730= Unifocalization MAPCA(s), Bilateral pulmonary unifocalization - Complete unifocalization (all usable MAPCA[s] are incorporated) ☐ 2740= Unifocalization MAPCA(s), Bilateral pulmonary unifocalization - Incomplete unifocalization (not all usable MAPCA[s] are incorporated) ☐ 2750= Unifocalization MAPCA(s), Unilateral pulmonary unifocalization ☐ 440= Unifocalization MAPCA(s) ☐ 450= Occlusion of MAPCA(s)
	Tricuspid Valve Disease and Ebstein's Anomaly	☐ 460= Valvuloplasty, Tricuspid (do not use this code if tricuspid valve malfunction is secondary to Ebstein's anomaly. Use 465= Ebstein's repair) ☐ 2280= Valvuloplasty converted to valve replacement in the same operation, Tricuspid ☐ 465= Ebstein's repair ☐ 470= Valve replacement, Tricuspid (TVR) ☐ 480= Valve closure, Tricuspid (exclusion, univentricular approach) ☐ 490= Valve excision, Tricuspid (without replacement) ☐ 500= Valve surgery, Other, Tricuspid
		☐ 510= RVOT procedure ☐ 520= 1 1/2 ventricular repair

	RVOT Obstruction, IVS Pulmonary Stenosis	☐ 530= PA, reconstruction (plasty), Main (trunk) ☐ 540= PA, reconstruction (plasty), Branch, Central (within the hilar bifurcation) ☐ 550= PA, reconstruction (plasty), Branch, Peripheral (at or beyond the hilar bifurcation) ☐ 570= DCRV repair
	Pulmonary Valve Disease	☐ 590= Valvuloplasty, Pulmonic ☐ 2270= Valvuloplasty converted to valve replacement in the same operation, Pulmonic ☐ 600= Valve replacement, Pulmonic (PVR) ☐ 630= Valve excision, Pulmonary (without replacement) ☐ 640= Valve closure, Semilunar ☐ 650= Valve surgery, Other, Pulmonic
Conduit operations	Conduit operations	☐ 610= Conduit placement, RV to PA ☐ 620= Conduit placement, LV to PA ☐ 1774= Conduit placement, Ventricle to aorta ☐ 1772= Conduit placement, Other
	Conduit Stenosis / Insufficiency	☐ 580= Conduit reoperation
Left Heart Lesions	Aortic Valve Disease	☐ 660= Valvuloplasty, Aortic ☐ 2240= Valvuloplasty converted to valve replacement in the same operation, Aortic ☐ 2310= Valvuloplasty converted to valve replacement in the same operation, Aortic – with Ross procedure ☐ 2320= Valvuloplasty converted to valve replacement in the same operation, Aortic – with Ross-Konno procedure ☐ 670= Valve replacement, Aortic (AVR) ☐ 680= Valve replacement, Aortic (AVR), Mechanical ☐ 690= Valve replacement, Aortic (AVR), Bioprosthetic ☐ 700= Valve replacement, Aortic (AVR), Homograft ☐ 715= Aortic root replacement, Bioprosthetic ☐ 720= Aortic root replacement, Mechanical ☐ 730= Aortic root replacement, Homograft ☐ 735= Aortic root replacement, Valve sparing ☐ 740= Ross procedure ☐ 750= Konno procedure ☐ 760= Ross-Konno procedure ☐ 770= Other annular enlargement procedure ☐ 780= Aortic stenosis, Subvalvar, Repair ☐ 2100= Aortic stenosis, Subvalvar, Repair, With myectomy for IHSS ☐ 790= Aortic stenosis, Supravalvar, Repair ☐ 800=Valve surgery, Other, Aortic
	Sinus of Valsalva Aneurysm	☐ 810= Sinus of Valsalva, Aneurysm repair
	LV to Aorta Tunnel	☐ 820= LV to aorta tunnel repair
	Mitral Valve Disease	☐ 830= Valvuloplasty, Mitral ☐ 2260= Valvuloplasty converted to valve replacement in the same operation, Mitral ☐ 840= Mitral stenosis, Supravalvar mitral ring repair ☐ 850= Valve replacement, Mitral (MVR) ☐ 860= Valve surgery, Other, Mitral
	Hypoplastic Left Heart and Related malformations	☐ 870= Norwood procedure ☐ 880= HLHS biventricular repair ☐ 2755= Conduit insertion right ventricle to pulmonary artery + Intraventricular tunnel left ventricle to neoaorta + arch reconstruction (Rastelli and Norwood type arch reconstruction) (Yasui)
Hybrid		☐ 2160= Hybrid Approach "Stage 1", Application of RPA & LPA bands

		☐ 2170= Hybrid Approach "Stage 1", Stent placement in arterial duct (PDA) ☐ 2180= Hybrid Approach "Stage 1", Stent placement in arterial duct (PDA) + application of RPA & LPA bands ☐ 2140= Hybrid approach "Stage 2", Aortopulmonary amalgamation + Superior Cavopulmonary anastomosis(es) + PA Debanding + Aortic arch repair (Norwood [Stage 1] + Superior Cavopulmonary anastomosis(es) + PA Debanding) ☐ 2150= Hybrid approach "Stage 2", Aortopulmonary amalgamation + Superior Cavopulmonary anastomosis(es) + PA Debanding + Without aortic arch repair ☐ 2760= Hybrid Approach, Transcardiac balloon dilatation ☐ 2770= Hybrid Approach, Transcardiac transcatheter device placement
Cardiomyopathy		☐ 890= Transplant, Heart ☐ 900= Transplant, Heart and lung ☐ 910= Partial left ventriculectomy (LV volume reduction surgery) (Batista)
Pericardial Disease		☐ 920= Pericardial drainage procedure ☐ 930= Pericardiectomy ☐ 940= Pericardial procedure, Other
Single Ventricle		☐ 950= Fontan, Atrio-pulmonary connection ☐ 960= Fontan, Atrio-ventricular connection ☐ 970= Fontan, TCPC, Lateral tunnel, Fenestrated ☐ 980= Fontan, TCPC, Lateral tunnel, Nonfenestrated ☐ 1000= Fontan, TCPC, External conduit, Fenestrated ☐ 1010= Fontan, TCPC, External conduit, Nonfenestrated ☐ 2780= Fontan, TCPC, Intra/extracardiac conduit, Fenestrated ☐ 2790= Fontan, TCPC, Intra/extracardiac conduit, Nonfenestrated ☐ 3310 = Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Fenestrated ☐ 3320 = Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Nonfenestrated ☐ 1025= Fontan revision or conversion (Re-do Fontan) ☐ 1030= Fontan, Other ☐ 2340= Fontan + Atrioventricular valvuloplasty ☐ 1035= Ventricular septation
Transposition of the Great Arteries	Congenitally Corrected TGA	☐ 1050=Congenitally corrected TGA repair, Atrial switch and ASO (double switch) ☐ 1060= Congenitally corrected TGA repair, Atrial switch and Rastelli ☐ 1070= Congenitally corrected TGA repair, VSD closure ☐ 1080= Congenitally corrected TGA repair, VSD closure and LV to PA conduit ☐ 1090= Congenitally corrected TGA repair, Other
	Transposition of the Great Arteries	☐ 1110= Arterial switch operation (ASO) ☐ 1120= Arterial switch operation (ASO) and VSD repair ☐ 1123= Arterial switch procedure + Aortic arch repair ☐ 1125= Arterial switch procedure and VSD repair + Aortic arch repair ☐ 1130= Senning ☐ 1140= Mustard ☐ 1145= Atrial baffle procedure, Mustard or Senning revision ☐ 1150= Rastelli ☐ 1160= REV ☐ 2190= Aortic root translocation over left ventricle (Including Nikaidoh procedure) ☐ 2210= TGA, Other procedures (Kawashima, LV-PA conduit, other)
DORV		☐ 1180= DORV, Intraventricular tunnel repair
DOLV		☐ 1200= DOLV repair
	Coarctation of Aorta and Aortic arch hypoplasia	☐ 1210= Coarctation repair, End to end ☐ 1220= Coarctation repair, End to end, Extended ☐ 1230= Coarctation repair, Subclavian flap

Thoracic Arteries and Veins		☐ 1240= Coarctation repair, Patch aortoplasty ☐ 1250= Coarctation repair, Interposition graft ☐ 1260= Coarctation repair, Other ☐ 1275= Coarctation repair + VSD repair ☐ 1280= Aortic arch repair ☐ 1285= Aortic arch repair + VSD repair
	Coronary Artery Anomalies	☐ 1290= Coronary artery fistula ligation ☐ 1291= Anomalous origin of coronary artery from pulmonary artery repair ☐ 1300= Coronary artery bypass ☐ 1305= Anomalous aortic origin of coronary artery (AAOCA) repair ☐ 1310= Coronary artery procedure, Other
	Interrupted Arch Patent Ductus Arteriosus	☐ 1320= Interrupted aortic arch repair ☐ 1330= PDA closure, Surgical ☐ 1340= PDA closure, Device
	Vascular Rings and Slings	☐ 1360= Vascular ring repair ☐ 1365= Aortopexy ☐ 1370= Pulmonary artery sling repair
	Aortic Aneurysm	☐ 1380= Aortic aneurysm repair
	Aortic Dissection	☐ 1390= Aortic dissection repair
Thoracic and Mediastinal Disease	Lung Disease	☐ 1400= Lung biopsy ☐ 1410= Transplant, lung(s) ☐ 1420= Lung procedure, Other
	Tracheal Stenosis	☐ 1440= Tracheal procedure
	Chest Wall	☐ 2800= Muscle flap, Trunk (i.e. intercostal, pectus, or serratus muscle) ☐ 2810= Muscle flap, Trunk (i.e. latissimus dorsi) ☐ 2820= Removal, Sternal wire ☐ 2830= Rib excision, Complete ☐ 2840= Rib excision, Partial ☐ 2850= Sternal fracture, Open treatment ☐ 2860= Sternal resection, Radical resection of the sternum ☐ 2870= Sternal resection, Radical resection of the sternum with mediastinal lymphadenectomy ☐ 2880= Tumor of chest wall, Excision including ribs ☐ 2890= Tumor of chest wall, Excision including ribs, With reconstruction ☐ 2900= Tumor of soft tissue of thorax, Excision of deep subfascial or intramuscular tumor ☐ 2910= Tumor of soft tissue of thorax, Excision of subcutaneous tumor ☐ 2920= Tumor of soft tissue of thorax, Radical resection
	Neck	☐ 2930= Hyoid myotomy and suspension ☐ 2940= Muscle flap, Neck ☐ 2950= Procedure on neck ☐ 2960= Tumor of soft tissue of neck, Excision of deep subfascial or intramuscular tumor ☐ 2970= Tumor of soft tissue of neck, Excision of subcutaneous tumor ☐ 2980= Tumor of soft tissue of neck, Radical resection
	Pectus Excavatum, Carinatum	☐ 2990= Pectus bar removal ☐ 3000= Pectus bar repositioning ☐ 3010= Pectus repair, Minimally invasive repair (Nuss), With thoracoscopy ☐ 3020= Pectus repair, Minimally invasive repair (Nuss), Without thoracoscopy ☐ 3030= Pectus repair, Open repair
	Thoracic Outlet	☐ 3040= Division of scalenus anticus, With resection of a cervical rib

		☐ 3050= Division of scalenus anticus, Without resection of a cervical rib ☐ 3060= Rib excision, Excision of a cervical rib ☐ 3070= Rib excision, Excision of a cervical rib, With sympathectomy ☐ 3080= Rib excision, Excision of first rib ☐ 3090= Rib excision, Excision of first rib, With sympathectomy
	Thorax	☐ 3100= Procedure on thorax
Electrophysiological		☐ 1450= Pacemaker implantation, Permanent ☐ 1460= Pacemaker procedure ☐ 2350= Explantation of pacing system ☐ 1470= ICD (AICD) implantation ☐ 1480= ICD (AICD) ([automatic] implantable cardioverter defibrillator) procedure ☐ 1490= Arrhythmia surgery - atrial, Surgical Ablation ☐ 1500= Arrhythmia surgery - ventricular, Surgical Ablation
Interventional Cardiology Procedures		☐ 2500= Cardiovascular catheterization procedure, Diagnostic ☐ 2520= Cardiovascular catheterization procedure, Diagnostic, Angiographic data obtained ☐ 2550= Cardiovascular catheterization procedure, Diagnostic, Electrophysiology alteration ☐ 2540= Cardiovascular catheterization procedure, Diagnostic, Hemodynamic alteration ☐ 2510= Cardiovascular catheterization procedure, Diagnostic, Hemodynamic data obtained ☐ 2530= Cardiovascular catheterization procedure, Diagnostic, Transluminal test occlusion ☐ 2410= Cardiovascular catheterization procedure, Therapeutic ☐ 2670= Cardiovascular catheterization procedure, Therapeutic, Adjunctive therapy ☐ 1540= Cardiovascular catheterization procedure, Therapeutic, Balloon dilation ☐ 2590= Cardiovascular catheterization procedure, Therapeutic, Balloon valvotomy ☐ 1580= Cardiovascular catheterization procedure, Therapeutic, Coil implantation ☐ 1560= Cardiovascular catheterization procedure, Therapeutic, Device implantation ☐ 3110= Cardiovascular catheterization procedure, Therapeutic, Device implantation attempted ☐ 2690= Cardiovascular catheterization procedure, Therapeutic, Electrophysiological ablation ☐ 3120= Cardiovascular catheterization procedure, Therapeutic, Intravascular foreign body removal ☐ 2640= Cardiovascular catheterization procedure, Therapeutic, Perforation (establishing interchamber and/or intervessel communication) ☐ 2580= Cardiovascular catheterization procedure, Therapeutic, Septostomy ☐ 1550= Cardiovascular catheterization procedure, Therapeutic, Stent insertion ☐ 2630= Cardiovascular catheterization procedure, Therapeutic, Stent re-dilation ☐ 2650= Cardiovascular catheterization procedure, Therapeutic, Transcatheter Fontan completion ☐ 2660= Cardiovascular catheterization procedure, Therapeutic, Transcatheter implantation of valve
Palliative Procedures		☐ 1590= Shunt, Systemic to pulmonary, Modified Blalock-Taussig Shunt (MBTS) ☐ 1600= Shunt, Systemic to pulmonary, Central (shunt from aorta) ☐ 3130= Shunt, Systemic to pulmonary, Central (shunt from aorta) Central shunt with an end-to-side connection between the transected main pulmonary artery and the side of the ascending aorta (i.e. Mee shunt) ☐ 3230= Shunt, Systemic to pulmonary, Potts – Smith type (descending aorta to pulmonary artery) ☐ 1610= Shunt, Systemic to pulmonary, Other ☐ 1630= Shunt, Ligation and takedown ☐ 2095= Shunt, Reoperation ☐ 1640= PA banding (PAB) ☐ 1650= PA debanding ☐ 3200= PA band adjustment

		☐ 1660= Damus-Kaye-Stansel procedure (DKS) (creation of AP anastomosis without arch reconstruction) ☐ 1670= Bidirectional cavopulmonary anastomosis (BDCPA) (bidirectional Glenn) ☐ 1680= Glenn (unidirectional cavopulmonary anastomosis) (unidirectional Glenn) ☐ 1690= Bilateral bidirectional cavopulmonary anastomosis (BBDCPA) (bilateral bidirectional Glenn) ☐ 1700= HemiFontan ☐ 2330= Superior cavopulmonary anastomosis(es) (Glenn or HemiFontan) + Atrioventricular valvuloplasty ☐ 2130= Superior Cavopulmonary anastomosis(es) + PA reconstruction ☐ 3300 = Takedown of superior cavopulmonary anastomosis ☐ 3140= Hepatic vein to azygous vein connection, Direct ☐ 3150= Hepatic vein to azygous vein connection, Interposition graft ☐ 3160= Kawashima operation (superior cavopulmonary connection in setting of interrupted IVC with azygous continuation) ☐ 1710= Palliation, Other
Fetal Interventions		☐ 3240=Attempted fetal intervention, percutaneous trans-catheter directed at interatrial septum ☐ 3250=Attempted fetal intervention, percutaneous trans-catheter directed at aortic valve ☐ 3260=Attempted fetal intervention, percutaneous trans-catheter directed at pulmonic valve ☐ 3270=Attempted fetal intervention "open" (maternal laparotomy with hysterotomy), directed at interatrial septum ☐ 3280=Attempted fetal intervention "open" (maternal laparotomy with hysterotomy), directed at aortic valve ☐ 3290=Attempted fetal intervention "open" (maternal laparotomy with hysterotomy), directed at pulmonic valve
Mechanical Support		☐ 2360= ECMO cannulation ☐ 2370= ECMO decannulation ☐ 1910= ECMO procedure ☐ 1900= Intraaortic balloon pump (IABP) insertion ☐ 1920= Right/left heart assist device procedure ☐ 2390= VAD explantation ☐ 2380= VAD implantation ☐ 3170= VAD change out
Anesthetic procedures		☐ 2420= Echocardiography procedure, Sedated transesophageal echocardiogram ☐ 2430= Echocardiography procedure, Sedated transthoracic echocardiogram ☐ 2435= Non-cardiovascular, Non-thoracic procedure on cardiac patient with cardiac anesthesia ☐ 2440= Radiology procedure on cardiac patient, Cardiac Computerized Axial Tomography (CT Scan) ☐ 2450= Radiology procedure on cardiac patient, Cardiac Magnetic Resonance Imaging (MRI) ☐ 2460= Radiology procedure on cardiac patient, Diagnostic radiology ☐ 2470= Radiology procedure on cardiac patient, Non-Cardiac Computerized Tomography (CT) on cardiac patient ☐ 2480= Radiology procedure on cardiac patient, Non-cardiac Magnetic Resonance Imaging (MRI) on cardiac patient ☐ 2490= Radiology procedure on cardiac patient, Therapeutic radiology

Miscellaneous Procedures		☐ 1720= Aneurysm, Ventricular, Right, Repair ☐ 1730= Aneurysm, Ventricular, Left, Repair ☐ 1740= Aneurysm, Pulmonary artery, Repair ☐ 1760= Cardiac tumor resection ☐ 1780= Pulmonary AV fistula repair/occlusion ☐ 1790= Ligation, Pulmonary artery ☐ 1802= Pulmonary embolectomy, Acute pulmonary embolus ☐ 1804= Pulmonary embolectomy, Chronic pulmonary embolus

		☐ 1810= Pleural drainage procedure ☐ 1820= Pleural procedure, Other ☐ 1830= Ligation, Thoracic duct ☐ 1840= Decortication ☐ 1850= Esophageal procedure ☐ 1860= Mediastinal procedure ☐ 1870= Bronchoscopy ☐ 1880= Diaphragm plication ☐ 1890= Diaphragm procedure, Other ☐ 1930= VATS (video-assisted thoracoscopic surgery) ☐ 1940= Minimally invasive procedure ☐ 1950= Bypass for noncardiac lesion ☐ 1960= Delayed sternal closure ☐ 1970= Mediastinal exploration ☐ 1980= Sternotomy wound drainage ☐ 3180= Intravascular stent removal ☐ 3220= Removal of transcatheter delivered device from heart ☐ 3210= Removal of transcatheter delivered device from blood vessel ☐ 1990= Thoracotomy, Other ☐ 2000= Cardiotomy, Other ☐ 2010= Cardiac procedure, Other ☐ 2020= Thoracic and/or mediastinal procedure, Other ☐ 2030= Peripheral vascular procedure, Other ☐ 2040= Miscellaneous procedure, Other ☐ 2050= Organ procurement ☐ 7777= Other procedure
Operation Canceled or Aborted	Canceled operation Aborted operation	☐ 7800= Operation canceled before skin incision ☐ 7810= Operation aborted after skin incision

PROCEDURE SPECIFIC FACTORS

Indicate if any of the following is the Primary procedure

☐ None of the listed procedures below *(if none, skip to Operative section)*

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ VSD repair, Primary closure
☐ VSD repair, Patch
☐ VSD repair, Device

Apical VSD	☐ Yes ☐ No
Straddling AV valve	☐ Yes ☐ No

If the following is the Primary procedure, specify whether the procedure specific factors apply

☐ TOF - AVC (AVSD) repair

Major coronary crossing RVOT - Coronary anomaly restricting RVOT enlargement	☐ Yes ☐ No
VSD, Multiple, Repair	☐ Yes ☐ No
Restrictive VSD	☐ Yes ☐ No
Hypoplastic branch pulmonary arteries (diminished pulmonary vascular bed)	☐ Yes ☐ No
AV Valve regurgitation grade 3 and 4 (Severe AV Valve regurgitation)	☐ Yes ☐ No
Double orifice left atrioventricular valve	☐ Yes ☐ No
Single papillary muscle in the left ventricle and/or parachute left atrioventricular valve	☐ Yes ☐ No
Hypoplastic posterior mural leaflet	☐ Yes ☐ No
Atrioventricular septal defect with ventricular imbalance: dominant left ventricle, hypoplastic right ventricle	☐ Yes ☐ No
Atrioventricular septal defect with ventricular imbalance: dominant right ventricle, hypoplastic left ventricle	☐ Yes ☐ No
Common atrioventricular valve with unbalanced commitment of valve to left ventricle	☐ Yes ☐ No
Common atrioventricular valve with unbalanced commitment of valve to right ventricle	☐ Yes ☐ No

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ TOF repair, No ventriculotomy
☐ TOF repair, Ventriculotomy, Nontransanular patch
☐ TOF repair, Ventriculotomy, Transanular patch
☐ TOF repair, RV-PA conduit
☐ TOF - Absent pulmonary valve repair
☐ Pulmonary atresia - VSD - MAPCA repair, Complete single stage repair (1-stage that includes bilateral pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit])
☐ Pulmonary atresia - VSD - MAPCA repair, Status post prior complete unifocalization (includes VSD closure + RV to PA connection [with or without conduit])
☐ Pulmonary atresia - VSD - MAPCA repair, Status post prior incomplete unifocalizarion (includes completion of pulmonary unifocalization + VSD closure + RV to PA connection [with or without conduit])
☐ Pulmonary atresia - VSD (including TOF, PA) repair

Major coronary crossing RVOT - Coronary anomaly restricting RVOT enlargement	☐ Yes ☐ No
VSD, Multiple, Repair	☐ Yes ☐ No
Restrictive VSD	☐ Yes ☐ No
Hypoplastic branch pulmonary arteries (diminished pulmonary vascular bed)	☐ Yes ☐ No

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ AVC (AVSD) repair, Complete (CAVSD)

AV Valve regurgitation grade 3 and 4 (Severe AV Valve regurgitation)	☐ Yes ☐ No
Double orifice left atrioventricular valve	☐ Yes ☐ No
Single papillary muscle in the left ventricle and/or parachute left atrioventricular valve	☐ Yes ☐ No
Hypoplastic posterior mural leaflet	☐ Yes ☐ No
Atrioventricular septal defect with ventricular imbalance: dominant left ventricle and hypoplastic right ventricle	☐ Yes ☐ No
Atrioventricular septal defect with ventricular imbalance: dominant right ventricle and hypoplastic left ventricle	☐ Yes ☐ No
Common atrioventricular valve with unbalanced commitment of valve to left ventricle	☐ Yes ☐ No
Common atrioventricular valve with unbalanced commitment of valve to right ventricle	☐ Yes ☐ No

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ Bidirectional cavopulmonary anastomosis (BDCPA) (bidirectional Glenn)
☐ Glenn (unidirectional cavopulmonary anastomosis) (unidirectional Glenn)
☐ Bilateral bidirectional cavopulmonary anastomosis (BBDCPA) (bilateral bidirectional Glenn)
☐ HemiFontan
☐ Superior Cavopulmonary anastomosis(es) (Glenn or HemiFontan) + Atrioventricular valvuloplasty
☐ Superior Cavopulmonary anastomosis(es) + PA reconstruction

AV Valve regurgitation grade 3 and 4 (Severe AV Valve regurgitation)	☐ Yes ☐ No
Moderate to severe systemic ventricular dysfunction	☐ Yes ☐ No
Hypoplastic branch pulmonary arteries (diminished pulmonary vascular bed)	☐ Yes ☐ No
Systemic ventricular outflow tract obstruction (subaortic obstruction)	☐ Yes ☐ No
Ventricular dominance	☐ Left Ventricular dominance ☐ Right Ventricular dominance ☐ Balanced ☐ Indeterminate Ventricular dominance

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ Fontan, Atrio-pulmonary connection
☐ Fontan, Atrio-ventricular connection
☐ Fontan, TCPC, Lateral tunnel, Fenestrated
☐ Fontan, TCPC, Lateral tunnel, Nonfenestrated
☐ Fontan, TCPC, External conduit, Fenestrated
☐ Fontan, TCPC, External conduit, Nonfenestrated
☐ Fontan, TCPC, Intra/extracardiac conduit, Fenestrated
☐ Fontan, TCPC, Intra/extracardiac conduit, Nonfenestrated
☐ Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Fenestrated
☐ Fontan, TCPC, External conduit, hepatic veins to pulmonary artery, Nonfenestrated
☐ Fontan, Other
☐ Fontan + Atrioventricular valvuloplasty
☐ Fontan revision or conversion (Re-do Fontan)

AV Valve regurgitation grade 3 and 4 (Severe AV Valve regurgitation)	☐ Yes ☐ No
Moderate to severe systemic ventricular dysfunction	☐ Yes ☐ No
Hypoplastic branch pulmonary arteries (diminished pulmonary vascular bed)	☐ Yes ☐ No
Systemic ventricular outflow tract obstruction (subaortic obstruction)	☐ Yes ☐ No
Ventricular dominance	☐ Left Ventricular dominance ☐ Right Ventricular dominance ☐ Balanced ☐ Indeterminate Ventricular dominance

If one of the following is the Primary procedure, specify whether the procedure specific factors apply

☐ Arterial switch operation (ASO)
☐ Arterial switch procedure + Aortic arch repair

Posterior coronary loop: circumflex coming off the RCA	☐ Yes ☐ No
Posterior coronary loop: left trunk coming off the RCA	☐ Yes ☐ No
Double coronary loops: inverted origin of right & left coronary arteries	☐ Yes ☐ No
Single coronary ostium	☐ Yes ☐ No
Intramural coronary	☐ Yes ☐ No
Large infundibular coronary artery from LAD	☐ Yes ☐ No
Malaligned commissures	☐ Yes ☐ No
Take down of a commissure	☐ Yes ☐ No
Aorto-pulmonary diameter mismatch	☐ Yes ☐ No
Side by side vessels	☐ Yes ☐ No
Posterior native aorta	☐ Yes ☐ No
Subaortic obstruction/ conal septum malalignment	☐ Yes ☐ No
Bicuspid native aortic valve (Bicuspid neopulmonary valve)	☐ Yes ☐ No
Bicuspid native pulmonary valve (Bicuspid neoaortic valve)	☐ Yes ☐ No

If one of the following is the Primary procedure, specify whether the procedure specific factors apply ☐ Arterial switch operation (ASO) and VSD repair ☐ Arterial switch procedure and VSD repair + Aortic arch repair		
	Posterior coronary loop: circumflex coming off the RCA	☐ Yes ☐ No
	Posterior coronary loop: left trunk coming off the RCA	☐ Yes ☐ No
	Double coronary loops: inverted origin of right & left coronary arteries	☐ Yes ☐ No
	Single coronary ostium	☐ Yes ☐ No
	Intramural coronary	☐ Yes ☐ No
	Large infundibular coronary artery from LAD	☐ Yes ☐ No
	Malaligned commissures	☐ Yes ☐ No
	Take down of a commissure	☐ Yes ☐ No
	Aorto-pulmonary diameter mismatch	☐ Yes ☐ No
	Side by side vessels	☐ Yes ☐ No
	Posterior native aorta	☐ Yes ☐ No
	Subaortic obstruction/ conal septum malalignment	☐ Yes ☐ No
	Bicuspid native aortic valve (Bicuspid neopulmonary valve)	☐ Yes ☐ No
	Bicuspid native pulmonary valve (Bicuspid neoaortic valve)	☐ Yes ☐ No
	Apical VSD	☐ Yes ☐ No
	Straddling AV valve	☐ Yes ☐ No
If one of the following is the Primary procedure, specify whether the procedure specific factors apply ☐ Truncus arteriosus repair ☐ Truncus + Interrupted aortic arch repair (IAA) repair		
	Truncus type 3 (PA Branches from PDA or descending aorta)	☐ Yes ☐ No
	Abnormal coronary	☐ Yes ☐ No
	Truncal valve regurgitation (moderate to severe)	☐ Yes ☐ No
	Truncal valve stenosis (moderate to severe)	☐ Yes ☐ No
If the following is the Primary procedure, specify whether the procedure specific factors apply ☐ Norwood procedure		
	Source of pulmonary blood flow: Shunt - systemic artery-to-pulmonary artery	☐ Yes ☐ No
	Source of pulmonary blood flow: Shunt - ventricle-to-pulmonary artery	☐ Yes ☐ No
	Source of pulmonary blood flow: Superior caval vein-to-pulmonary artery	☐ Yes ☐ No
	Ascending aorta < 2 mm	☐ Yes ☐ No
	Aortic atresia	☐ Yes ☐ No
	Aortic stenosis	☐ Yes ☐ No
	Mitral atresia	☐ Yes ☐ No
	Mitral stenosis	☐ Yes ☐ No
	Sinusoids	☐ Yes ☐ No
	Intact atrial septum	☐ Yes ☐ No
	Obstructed pulmonary venous return with severely restrictive ASD	☐ Yes ☐ No
	AV Valve regurgitation grade 3 and 4 (Severe AV Valve regurgitation)	☐ Yes ☐ No
	Aberrant right subclavian artery	☐ Yes ☐ No
	Ventricular dominance ☐ Left Ventricular dominance ☐ Right Ventricular dominance ☐ Balanced ☐ Indeterminate Ventricular dominance	

If the following is the Primary procedure, specify whether the procedure specific factors apply		
☐ Ebstein's repair		
	Tricuspid Valve Repair	☐ Yes ☐ No
If Yes→	Monocusp	☐ Yes ☐ No
	Bileaflet repair	☐ Yes ☐ No
	Cone repair (360° leaflet approximation)	☐ Yes ☐ No
	Sebening stitch (anterior RV papillary muscle to ventricular septum)	☐ Yes ☐ No
	Annular reduction	☐ Yes ☐ No
If Yes→	Plication	☐ Yes ☐ No
	Partial ring (c-shaped anterior & inferior annulus)	☐ Yes ☐ No
	Eccentric ring (inferior annulus)	☐ Yes ☐ No
	Atrialized RV plication	☐ Yes ☐ No
	Atrialized RV resection	☐ Yes ☐ No
	ASD/PFO closure	☐ Yes ☐ No ☐ Subtotal
	Reduction atrioplasty	☐ Yes ☐ No
	Arrhythmia surgery	☐ Yes ☐ No
If Yes→	Cavotricuspid isthmus ablation	☐ Yes ☐ No
	Modified right atrial maze	☐ Yes ☐ No
	Left atrial Cox maze	☐ Yes ☐ No
	Pulmonary vein isolation	☐ Yes ☐ No
	Bidirectional cavopulmonary anastomosis	☐ Yes ☐ No

OPERATIVE

Procedure Location:	☐ Cardiac OR	☐ ICU	☐ SICU	
	☐ General OR	☐ CVICU	☐ Radiology Suite	
	☐ Hybrid Suite	☐ NICU	☐ Procedure Room	
	☐ Cath lab	☐ PICU	☐ Other	
Status:	☐ Elective	☐ Urgent	☐ Emergent	☐ Salvage
Operation Type:	☐ CPB Cardiovascular	☐ No CPB Cardiovascular	☐ CPB Non-Cardiovascular	
	☐ ECMO	☐ Thoracic	☐ Interventional Cardiology	
	☐ VAD with CPB	☐ VAD without CPB	☐ NonCardiac/NonThoracic Procedure w/ Anesthesia	
	☐ Other			

Near InfraredSpectroscopy (NIRS) Cerebral Metrics Used:		☐ Yes ☐ No
If NIRSCerUsed is Yes→	NIRS Cerebral Metrics Used Preoperatively	☐ Yes ☐ No
	NIRS Cerebral Metrics Used Intraoperatively	☐ Yes ☐ No
	NIRS Cerebral Metrics Used Postoperatively	☐ Yes ☐ No
Near InfraredSpectroscopy (NIRS) Somatic Metrics Used:		☐ Yes ☐ No
If NIRSSomUsed is Yes→	NIRS Somatic Metrics Used Preoperatively	☐ Yes ☐ No
	NIRS Somatic Metrics Used Intraoperatively	☐ Yes ☐ No
	NIRS Somatic Metrics Used Postoperatively	☐ Yes ☐ No

OR Entry Time: *(00:00 – 23:59)* __ __: __ __ Skin Incision Start Time: *(00:00 – 23:59)* __ __: __ __

Endotracheal Intubation Performed: ☐ Yes ☐ No *(If Yes ↓)*

Intubation Date/Time: *(mm/dd/yyyy 00:00 – 23:59)* __ __ / __ __ / __ __ __ __ __ __:__ __

Initial Extubation Date/Time: *(mm/dd/yyyy 00:00 – 23:59)* __ __ / __ __ / __ __ __ __ __ __:__ __

Extubated in OR: ☐ Yes ☐ No

Re-Intubated After Initial Postoperative Extubation: ☐ Yes ☐ No *(If Yes ↓)*

Final Extubation Date/Time: *(mm/dd/yyyy 00:00 – 23:59)* __ __ / __ __ / __ __ __ __ __ __:__ __

Time of Skin Closure: *(00:00 – 23:59)* __ __:__ __ OR Exit Time: *(00:00 – 23:59)* __ __:__ __ Extended Through Midnight: ☐ Yes ☐ No

If Op type is: "NonCardiac/NonThoracic Procedure w/Anesthesia" or "Interventional Cardiology" → Skip to Complications section.

Surgeon:	Surgeon NPI:	Taxpayer Identification Number:

Reoperation Within This Admission: ☐ Yes – Planned reoperation ☐ Yes – Unplanned reoperation ☐ No

Number of Prior Cardiothoracic Operations:	Number of Prior CPB Cardiothoracic Operations:

(If operation type is No CPB Cardiovascular→) Cross Clamp Time – No CPB: *(minutes):*

(If operation type is CPB Cardiovascular or VAD w/ CPB or CPB NonCardiovascular√)

CPB Blood Prime: ☐ Yes ☐ No CPB Time *(min)*:_____ Cross Clamp Time - CPB:*(min)*:_____ Circulatory Arrest Time *(min)*:_____

Patient Temperature Monitoring Site :

		(If Yes →) (If Yes, Lowest Core Temperature recorded at site):
Bladder:	☐ Yes ☐ No	_____ °C
Esophageal:	☐ Yes ☐ No	_____ °C
Nasopharyngeal:	☐ Yes ☐ No	_____ °C
Rectal:	☐ Yes ☐ No	_____ °C
Tympanic:	☐ Yes ☐ No	_____ °C
Other:	☐ Yes ☐ No	_____ °C

Cooling Time: *(minutes)* _____ Rewarming Time: *(minutes)* _____

Cerebral Perfusion Utilized: ☐ Yes ☐ No *(If Yes √)*

Cerebral Perfusion Time: _____ *(minutes)*

Cerebral Perfusion Cannulation Site:

Innominate Artery	☐ Yes ☐ No	Right Subclavian	☐ Yes ☐ No
Right Axillary Artery	☐ Yes ☐ No	Right Carotid Artery	☐ Yes ☐ No
Left Carotid Artery	☐ Yes ☐ No	Superior Vena Cava	☐ Yes ☐ No

Cerebral Perfusion Periods: _____

Cerebral Perfusion Flow Rate: _____ *(mL/kg) per minute*

Cerebral Perfusion Temperature: _____ °C

Arterial Blood Gas Management During Cooling: ☐ Alpha STAT ☐ pH STAT ☐ pHSTAT cooling/Alpha STAT rewarming ☐ Other Combination

Hematocrit Prior to Circulatory Arrest or Cerebral Perfusion: _____

Cardioplegia Delivery: ☐ None ☐ Antegrade ☐ Retrograde ☐ Both

If CPlegiaDeliv is Antegrade, Retrograde or Both √

Cardioplegia Type: ☐ Blood ☐ Crystalloid ☐ Both ☐ Other

Cardioplegia Solution:

☐ del Nido	☐ Celsior
☐ Custodiol / Bretschneider (HTK)	☐ Roe's Solution
☐ Buckberg	☐ Microplegia with Potassium
☐ Plegisol / St. Thomas	☐ Microplegia with Adenocaine
☐ University of Wisconsin	☐ Other

Cardioplegia Number of Doses: _____

Hematocrit - First after initiating CPB: _____

Hematocrit - Last Measured During CPB: _____

Hematocrit – Post CPB, Post Protamine: _____

Ultrafiltration performed After CPB:
☐ No
☐ Yes, Modified Ultrafiltration (MUF)
☐ Yes, Conventional Ultrafiltration (CUF)
☐ Yes, MUF and CUF

Pulmonary Vascular Resistance Measured: ☐ Yes ☐ No

(If Yes and WeightKg ≥40 →) PVR: _____ *(Wood units)*

(If Yes and WeightKg <40 →) PVR Index: _____ *(Wood units x m2)*

Blood and Blood Related Products (Including CPB Blood Prime Units)

Autologous Transfusion: ☐ Yes ☐ No | Cell Saver/Salvage Reinfused: ☐ Yes ☐ No

Transfusion of Non-Autologous Blood Products During or After Procedure: ☐ Yes ☐ No ☐ Patient/family refused

(If Yes →) Transfusion of Blood Products During Procedure: ☐ Yes ☐ No *(If Yes √)*

# Units Packed Red Blood Cells	_____ *(0-100)*	# Units Fresh Frozen Plasma	_____ *(0-100)*
# Units Fresh Plasma	_____ *(0-100)*	# Units Single Donor Pheresis Platelets	_____ *(0-100)*
# Units Individual Platelets	_____ *(0-100)*	# Units Cryoprecipitate	_____ *(0-100)*
# Units Fresh Whole Blood	_____ *(0-100)*	# Units Whole Blood	_____ *(0-100)*

(If Yes →) Transfusion of Blood Products within 24 hours post procedure: ☐ Yes ☐ No *(If Yes √)*

# Units Packed Red Blood Cells	_____ *(0-100)*	# Units Fresh Frozen Plasma	_____ *(0-100)*
# Units Fresh Plasma	_____ *(0-100)*	# Units Single Donor Pheresis Platelets	_____ *(0-100)*
# Units Individual Platelets	_____ *(0-100)*	# Units Cryoprecipitate	_____ *(0-100)*
# Units Fresh Whole Blood	_____ *(0-100)*	# Units Whole Blood	_____ *(0-100)*

(If Yes →) Transfusion of Blood Products after 24 hours post procedure: ☐ Yes ☐ No (If Yes ↓)

# Units Packed Red Blood Cells	(0-100)	# Units Fresh Frozen Plasma	(0-100)
# Units Fresh Plasma	(0-100)	# Units Single Donor Pheresis Platelets	(0-100)
# Units Individual Platelets	(0-100)	# Units Cryoprecipitate	(0-100)
# Units Fresh Whole Blood	(0-100)	# Units Whole Blood	(0-100)

(If Yes →) Directed Donor Units: ☐ Yes ☐ No

Antifibrinolytics Used Intraoperatively: ☐ Yes ☐ No

(If Yes →) Epsilon Amino-Caproic Acid (Amicar, EACA) Used: ☐ Yes ☐ No

(If Yes →) Epsilon Amino-Caproic Acid (Amicar, EACA) Load mg/kg: (0-300)

Epsilon Amino-Caproic Acid (Amicar, EACA) Pump Prime mg/kg: (0-300)

(If AntifinEpPrime >0) Was Epsilon Amino-Caproic Acid (Amicar, EACA) dosed as mg/ml of Pump Prime: ☐ Yes ☐ No ☐ Unknown

Epsilon Amino-Caproic Acid (Amicar, EACA) Infusion rate mg/kg/hr:: (0-200)

Tranexamic Acid Used: ☐ Yes ☐ No

(If Yes →) Tranexamic Acid Load mg/kg: (0-150)

Tranexamic Acid Pump Prime mg/kg: (0-150)

(If AntifibTranexPrime >0) Was Tranexamic Acid dosed as mg/ml of Pump Prime: ☐ Yes ☐ No ☐ Unknown

Tranexamic Acid Infusion rate mg/kg/hr:: (0-50)

Trasylol (Aprotinin) Used: ☐ Yes ☐ No

(If Yes →) Trasylol (Aprotinin) Load cc/kg: (0-10)

Trasylol (Aprotinin) Pump Prime cc/kg: (0-10)

Trasylol (Aprotinin) Infusion rate cc/kg/hr:: (0-10)

Procoagulent Used Intraoperatively: ☐ Yes ☐ No

(If Yes →) Factor VIIa (Novoseven) Usage: ☐ Yes ☐ No

(If Yes →) Factor VIIa (Novoseven) mcg/kg Dose 1: (1-200)

Factor VIIa (Novoseven) mcg/kg Dose 2: (0-200)

(If Dose 2 > 0 →) Factor VIIa (Novoseven) mcg/kg Dose 3: (0-200)

Prothrombin Complex Concentrate-4 (PCC-4, KCentra) Usage: ☐ Yes ☐ No

(If Yes →) Prothrombin Complex Concentrate-4 (PCC-4, KCentra) units/kg Dose 1: (1-100)

Prothrombin Complex Concentrate-4 (PCC-4, KCentra) units/kg Dose 2: (0-100)

(If Dose 2 > 0 →) Prothrombin Complex Concentrate-4 (PCC-4, KCentra) units/kg Dose 3: (0-100)

Prothrombin Complex Concentrate-4 with Factor VIIa (FEIBA) Usage: ☐ Yes ☐ No

(If Yes →) Prothrombin Complex Concentrate-4 with Factor VIIa (FEIBA) units/kg Dose 1: (1-200)

Prothrombin Complex Concentrate-4 with Factor VIIa (FEIBA) units/kg Dose 2: (0-200)

(If Dose 2 > 0 →) Prothrombin Complex Concentrate-4 with Factor VIIa (FEIBA) units/kg Dose 1: (0-200)

Prothrombin Complex Concentrate-3 (PCC-3, ProfilNine-SD) Usage: ☐ Yes ☐ No

(If Yes →) Prothrombin Complex Concentrate-3 (PCC-3, ProfilNine-SD) units/kg Dose 1: (1-5)

Prothrombin Complex Concentrate-3 (PCC-3, ProfilNine-SD) units/kg Dose 2: (0-5)

(If Dose 2 > 0 →) Prothrombin Complex Concentrate-3 (PCC-3, ProfilNine-SD) units/kg Dose 3: (0-5)

Octaplex Prothrombin Concentrate Usage: ☐ Yes ☐ No
(If Yes →) Octaplex Prothrombin Concentrate – units Dose 1: _____ (1-6000)
Octaplex Prothrombin Concentrate – units Dose 2: _____ (0-6000)
(If Dose 2 > 0 →) Octaplex Prothrombin Concentrate – units Dose 3: _____ (0-6000)

Fibrinogen Concentrate Usage: ☐ Yes ☐ No
(If Yes →) Fibrinogen Concentrate mg/kg – Dose 1 _____ (1-100)
Fibrinogen Concentrate mg/kg – Dose 2 _____ (0-100)
(If Dose 2 > 0 →) Fibrinogen Concentrate mg/kg – Dose 3 _____ (0-100)

Antithrombin 3 Concentrate (AT3) Usage: ☐ Yes ☐ No
(If Yes →) Antithrombin 3 Concentrate (AT3) units Dose 1: _____ (1-5000)
Antithrombin 3 Concentrate (AT3) units Dose 2: _____ (0-5000)
(If Dose 2 > 0 →) Antithrombin 3 Concentrate (AT3) units Dose 3 _____ (0-5000)

Desmopressin (DDAVP) Usage: ☐ Yes ☐ No
(If Yes →) Desmopressin (DDAVP) mcg/kg Dose 1: _____ (0.01-6.00)
Desmopressin (DDAVP) mcg/kg Dose 2: _____ (0-6.00)
(If Dose 2 > 0 →) Desmopressin (DDAVP) mcg/kg Dose 3: _____ (0-6.00)

Point of Care Coagulation Testing Used Intraoperatively: ☐ Yes ☐ No
(If Yes →)
Thromboelastography (TEG): ☐ Yes ☐ No
ROTEM: ☐ Yes ☐ No
Sonoclot: ☐ Yes ☐ No
Heparin Concentration (Hepcon, HMS): ☐ Yes ☐ No
INR/PT/aPPP (iStat or equivalent): ☐ Yes ☐ No

CABG PROCEDURES

If Op Type is CBP or No CBP Cardiovascular ↓

Coronary Artery Bypass (CAB): ☐ Yes ☐ No *(If Yes ↓)*

Number of Distal Arterial Anast: _____ Number of Distal Vein Anast: _____

Internal Mammary Artery (IMA) Used:
☐ Left IMA ☐ Right IMA
☐ Both IMAs ☐ No IMA

VALVE PROCEDURES

If Op Type is CBP or No CBP Cardiovascular ↓

Valve Operation: ☐ Yes ☐ No *(If Yes ↓)*

Valve Device Explanted and/or Implanted: ☐ No ☐ Yes, Explanted ☐ Yes, Implanted ☐ Yes, Explanted and Implanted

If Yes, Explanted orYes, explanted and Implanted, complete one column per explant ↓

EXPLANT(S)

Valve Explant #1	**2nd Explant: ☐ Yes ☐ No**	**3rd Explant: ☐ Yes ☐ No**	**4th Explant: ☐ Yes ☐ No**
	If Yes ↓ (if no skip to implant)	*If Yes ↓ (if no skip to implant)*	*If Yes ↓ (if no skip to implant)*
Valve Explant Type #1	Valve Explant Type #2	Valve Explant Type #3	Valve Explant Type #4
☐ Mechanical	☐ Mechanical	☐ Mechanical	☐ Mechanical
☐ Bioprosthetic	☐ Bioprosthetic	☐ Bioprosthetic	☐ Bioprosthetic
☐ Homograft/Allograft	☐ Homograft/Allograft	☐ Homograft/Allograft	☐ Homograft/Allograft
☐ Autograft	☐ Autograft	☐ Autograft	☐ Autograft
☐ Annuloplasty Band/Ring	☐ Annuloplasty Band/Ring	☐ Annuloplasty Band/Ring	☐ Annuloplasty Band/Ring
☐ Mitral Clip	☐ Mitral Clip	☐ Mitral Clip	☐ Mitral Clip
☐ Surgeon Fashioned	☐ Surgeon Fashioned	☐ Surgeon Fashioned	☐ Surgeon Fashioned
☐ Other	☐ Other	☐ Other	☐ Other
Valve Explant #1 UDI:	Valve Explant #2 UDI:	Valve Explant #3 UDI:	Valve Explant #4 UDI:
_____	_____	_____	_____

If Yes, Implanted or Yes, Explanted and Implanted, complete one column per implant ↓

IMPLANT(S)

Valve Implant Location #1	**2nd Implant: ☐ Yes ☐ No**	**3rd Implant: ☐ Yes ☐ No**	**4th Implant: ☐ Yes ☐ No**
	If Yes ↓ (if no skip to VAD proc)	*If Yes ↓ (if no skip to VAD proc)*	*If Yes ↓ (if no skip to VAD proc)*
	Valve Implant Location #2	Valve Implant Location #3	Valve Implant Location #4
☐ Aortic	☐ Aortic	☐ Aortic	☐ Aortic
☐ Mitral	☐ Mitral	☐ Mitral	☐ Mitral
☐ Tricuspid	☐ Tricuspid	☐ Tricuspid	☐ Tricuspid
☐ Pulmonic	☐ Pulmonic	☐ Pulmonic	☐ Pulmonic
☐ Common AV	☐ Common AV	☐ Common AV	☐ Common AV
☐ Truncal	☐ Truncal	☐ Truncal	☐ Truncal
Valve Implant Type #1	Valve Implant Type #2	Valve Implant Type #3	Valve Implant Type #4
☐ Surgeon Fashioned	☐ Surgeon Fashioned	☐ Surgeon Fashioned	☐ Surgeon Fashioned
☐ Autograft	☐ Autograft	☐ Autograft	☐ Autograft
☐ Commercially supplied	☐ Commercially supplied	☐ Commercially supplied	☐ Commercially supplied
If Surgeon fashioned ↓	*If Surgeon fashioned ↓*	*If Surgeon fashioned ↓*	*If Surgeon fashioned ↓*
Material #1:	Material #2:	Material #3:	Material #4:
☐ PTFE (Gore-Tex)	☐ PTFE (Gore-Tex)	☐ PTFE (Gore-Tex)	☐ PTFE (Gore-Tex)
☐ Pericardium	☐ Pericardium	☐ Pericardium	☐ Pericardium
☐ Other	☐ Other	☐ Other	☐ Other
If Commercially Supplied↓	*If Commercially Supplied↓*	*If Commercially Supplied↓*	*If Commercially Supplied↓*
Model #1:_____	Model #2:_____	Model #3: _____	Model #4: _____
Device Size #1: ____	Device Size #2: ____	Device Size #3: ____	Device Size #4: ____
UDI#1_____	UDI#2_____	UDI#3_____	UDI#4_____

VAD PROCEDURES

VAD Explanted and/or Implanted: ☐ No ☐ Yes, Explanted ☐ Yes, Implanted ☐ Yes, Explanted and Implanted

If Implanted or Explanted and Implanted ↓

Indication: ☐ Bridge to Transplantation ☐ Bridge to Recovery ☐ Destination
☐ Postcardiotomy Ventricular failure ☐ Device malfunction ☐ End of Life

Implant Type: ☐ RVAD ☐ LVAD ☐ BiVAD ☐ TAH (total artificial heart)

Product: (choose from VAD List) _____

Implant UDI: _____

If Explanted or Explanted and Implanted ↓

Explant Reason: ☐ Cardiac Transplant ☐ Recovery ☐ Device Transfer
☐ Device Related Infection ☐ Device Malfunction ☐ End of Life

Explant UDI: _____

If Explanted, Implanted or Explanted and Implanted indicate whether VAD related complications occurred↓

Intracranial Bleed:	☐ Yes ☐ No	Embolic Stroke:	☐ Yes ☐ No	Driveline/Cannula Infection:	☐ Yes ☐ No
Pump Pocket Infection:	☐ Yes ☐ No	Endocarditis:	☐ Yes ☐ No	Device Malfunction:	☐ Yes ☐ No
Bowel Obstruction:	☐ Yes ☐ No	Hemolysis:	☐ Yes ☐ No		

COMPLICATIONS

Assign complication(s) to the operation that is most closely associated with the complication

☐ 15= No complications *OR select ALL that apply: (√)*

☐ 16= No complications during the intraop or postop time periods (No complications prior to discharge & no complications within ≤ 30 days of surgery)

- ☐ 350= Intraoperative death or intraprocedural death
- ☐ 360= Unplanned readmission to the hospital within 30 days of surgery or intervention
- ☐ 370= Multi-System Organ Failure (MSOF) = Multi-Organ Dysfunction Syndrome (MODS)
- ☐ 30= Unexpected Cardiac arrest during or following procedure (Periop/Periprocedural = Intraop/Intraprocedural and/or Postop/Postprocedural)
- ☐ 80= Cardiac dysfunction resulting in low cardiac output
- ☐ 384= Cardiac failure (severe cardiac dysfunction)
- ☐ 280= Endocarditis-postprocedural infective endocarditis
- ☐ 110= Pericardial effusion, Requiring drainage
- ☐ 390= Pulmonary hypertension
- ☐ 140= Pulmonary hypertensive crisis (PA pressure > systemic pressure)
- ☐ 130= Pulmonary vein obstruction
- ☐ 120= Systemic vein obstruction
- ☐ 240= Bleeding, Requiring reoperation
- ☐ 102= Sternum left open, Planned
- ☐ 104= Sternum left open, Unplanned
- ☐ 22= Unplanned cardiac reoperation during the postoperative or postprocedural time period, exclusive of reoperation for bleeding
- ☐ 24= Unplanned interventional cardiovascular catheterization procedure during the postoperative or postprocedural time period
- ☐ 26= Unplanned non-cardiac reoperation during the postoperative or postprocedural time period
- ☐ 40= Postoperative/Postprocedural mechanical circulatory support (IABP, VAD, ECMO, or CPS)
- ☐ 72= Arrhythmia requiring drug therapy
- ☐ 73= Arrhythmia requiring electrical cardioversion or defibrillation
- ☐ 74= Arrhythmia necessitating pacemaker, Permanent pacemaker
- ☐ 75= Arrhythmia necessitating pacemaker, Temporary pacemaker
- ☐ 210= Chylothorax
- ☐ 200= Pleural effusion, Requiring drainage
- ☐ 180= Pneumonia
- ☐ 190= Pneumothorax, Requiring drainage or evacuation
- ☐ 150= Postoperative/Postprocedural respiratory insufficiency requiring mechanical ventilatory support > 7 days
- ☐ 160= Postoperative/Postprocedural respiratory insufficiency requiring reintubation
- ☐ 170= Respiratory failure, Requiring tracheostomy
- ☐ 230= Renal failure - acute renal failure, Acute renal failure requiring dialysis at the time of hospital discharge
- ☐ 223= Renal failure - acute renal failure, Acute renal failure requiring temporary dialysis with the need for dialysis not present at hospital discharge
- ☐ 224= Renal failure - acute renal failure, Acute renal failure requiring temporary hemofiltration with the need for dialysis not present at hospital discharge
- ☐ 290= Sepsis
- ☐ 320= Neurological deficit, Neurological deficit persisting at discharge
- ☐ 325= Neurological deficit, Transient neurological deficit not present at discharge
- ☐ 300= Paralyzed diaphragm (possible phrenic nerve injury)
- ☐ 400= Peripheral nerve injury, Neurological deficit persisting at discharge
- ☐ 331= Seizure
- ☐ 410= Spinal cord injury, Neurological deficit persisting at discharge
- ☐ 420= Stroke
- ☐ 440= Subdural Bleed
- ☐ 450= Intraventricular hemorrhage (IVH) > grade 2
- ☐ 470= Thrombus, Intracardiac
- ☐ 480= Thrombus, Central vein
- ☐ 510= Thrombosis/thromboembolism, Pulmonary artery
- ☐ 490= Thrombus, Peripheral deep vein
- ☐ 500= Thrombosis, Systemic to pulmonary shunt
- ☐ 310= Vocal cord dysfunction (possible recurrent laryngeal nerve injury)
- ☐ 250= Wound dehiscence (sterile)
- ☐ 255= Wound dehiscence (sterile), Median sternotomy
- ☐ 520= Sternal instability (sterile)
- ☐ 261= Wound infection

☐ 262= Wound infection-Deep wound infection
☐ 270= Wound infection-Mediastinitis
☐ 263= Wound infection-Superficial wound infection
☐ 430= Anesthesia – related complication
☐ 460= Complication of cardiovascular catheterization procedure
☐ 900= Other complication
☐ 901= Other operative/procedural complication

DISCHARGE/READMISSION

Date of Hospital Discharge: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __
Mortality Status at Hospital Discharge: ☐ Alive ☐ Dead
(If Alive →) Discharge Location: ☐ Home ☐ Other Acute Care Center ☐ Other Chronic Care Center
VAD Discharge Status: ☐ No VAD this admission ☐ Discharged w/ VAD ☐ VAD removed prior to discharge ☐ Expired in Hospital
Date of Database Discharge: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __
Mortality Status at Database Discharge: ☐ Alive ☐ Dead ☐ Unknown *(If Alive ↓)*
Readmission within 30 days: ☐ Yes ☐ No *(If Yes →)* Readmission Date: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __
(If Yes →) Primary Readmission Reason *(select one↓):*

☐ Thrombotic Complication	☐ Neurologic Complication
☐ Hemorrhagic Complication	☐ Respiratory Complication/Airway Complication
☐ Stenotic Complication	☐ Septic/Infectious Complication
☐ Arrhythmia	☐ Cardiovascular Device Complications
☐ Congestive Heart Failure	☐ Residual/Recurrent Cardiovascular Defects
☐ Embolic Complication	☐ Failure to Thrive
☐ Cardiac Transplant Rejection	☐ VAD Complications
☐ Myocardial Ischemia	☐ Gastrointestinal Complication
☐ Renal Failure	☐ Other Cardiovascular Complication
☐ Pericardial Effusion and/or Tamponade	☐ Other - Readmission related to this index operation
☐ Pleural Effusion	☐ Other - Readmission not related to this index operation

Status at 30 days after surgery: ☐ Alive ☐ Dead ☐ Unknown
30 Day Status Method of Verification: ☐ Evidence of life or death in Medical Record ☐ Contact w/ patient or family
☐ Contact w/ medical provider ☐ Office visit to provider ≥ 30 days post op ☐ SSDMF ☐Other
Operative Mortality: ☐ Yes ☐ No
CHSS Eligibility: ☐ Eligible & Enrolled ☐ Eligible, but declined enrollment ☐ Eligible, but not invited to participate
☐ Eligible, but institution not CHSS participant ☐ Eligible, but not enrolled, other reason ☐ Not Eligible

PATIENT PROCESS MEASURES

(if Op Type CPB , No CPB Cardiovascular , or CPB Noncardiovascular ↓)
Patient care discussed at preop multidisciplinary planning conference: ☐ Yes ☐ No
If No → Reason care was not discussed: ☐ Urgent/Emergent/Salvage Case ☐ Patient admitted between conferences
☐ Program does not routinely discuss all cases ☐ Program does not have regular conferences
☐ Other
Transesophageal Echo (TEE) available for case: ☐ Yes ☐ No
If Yes → Intraop TEE performed: ☐ Yes ☐ No
Pre-op Antibiotic Prophylaxis given: ☐ Yes ☐ No
If Yes → Cephalosporin ☐ Yes ☐ No Penicillin or related med ☐ Yes ☐ No Aminoglycoside ☐ Yes ☐ No
Vancomycin ☐ Yes ☐ No Other ☐ Yes ☐ No
Antibiotic Start time: *(00:00 – 23:59)* _ _:_ _

Conventional Pre-procedure Time Out: ☐ Yes ☐ No

Surgeon shares essential elements of operative plan: ☐ Yes ☐ No

Postprocedure debriefing: ☐ Yes ☐ No

Hand-off protocol at the time of transfer to ICU:
☐ Yes- all required team members present
☐ Yes- not all required team members present
☐ No

If yes-not all required team members present →

Anesthesiologist:	☐ Attended hand-off	☐ Did not attend hand-off
Surgeon:	☐ Attended hand-off	☐ Did not attend hand-off
ICU MD:	☐ Attended hand-off	☐ Did not attend hand-off
Nurse:	☐ Attended hand-off	☐ Did not attend hand-off

Patient died or had major postoperative complication(s): ☐ Yes ☐ No

If Yes → Management and outcomes reviewed:
☐ Reviewed at conference
☐ Scheduled for review at conference
☐ Not reviewed or scheduled for review
☐ Program does not have scheduled conferences

If Reviewed → Review Date: *(mm/dd/yyyy)* __ __ / __ __ / __ __ __ __

STS National Database
Using data to drive quality

ANESTHESIA
(for sites participating in CHSD anesthesiology component)

ANESTHESIA Administrative

Anesthesiologist Present: ☐ Yes ☐ No

Primary Anesthesiologist Attending: _____

(If Yes→) Primary Anesthesiologist National Provider Identifier: _____

Secondary Anesthesiologist Attending: ☐ Yes ☐ No

Fellow or Resident Present ☐ Yes ☐ No

Mid-Level provider CRNA/AA Present ☐ Yes ☐ No

ANESTHESIA Preoperative

Preoperative Medication Category: (within 24 hours unless listed otherwise)

☐ 5= None *(If not None, select all pre-operative medications that apply: ↓)*

☐ 10= Amiodarone	☐ 190= Heparin
☐ 20= Angiotension Converting Enzyme (ACE) Inhibitors	☐ 220= Heparin, Low molecular weight
☐ 760= Angiotension Receptor Blockers (ARB)	☐ 710= Inotropes Not Otherwise Listed
☐ 700= Anti-arrhythmics Not Otherwise Listed	☐ 210= Insulin
☐ 770= Anticoagulents Not Otherwise Listed	☐ 230= Milrinone
☐ 30= Anti-reflux Meds (H2 antagonists,PPI, propulsives)	☐ 240= Narcotics
☐ 40= Anti-seizure medications	☐ 250= Nitric Oxide
☐ 50= Aspirin (within 5 days)	☐ 260= Nitroglycerin
☐ 60= Benzodiazepines	☐ 270= Nitroprusside
☐ 70= Beta Blockers	☐ 280= Norepinephrine (Levophed)
☐ 80= Birth Control (Oral, IM)	☐ 290= PDE-5 Inhibitors (e.g., Sildenafil)
☐ 200= Bronchodilators, Inhaled	☐ 300= Platelet inhibitors other than Aspirin (e.g.,Plavix) (within 5 days)
☐ 90= Calcium Channel Blockers	☐ 310= Prostacyclin (e.g., Flolan, Remodulin)
☐ 100= Calcium Chloride Infusion	☐ 320= Prostaglandin
☐ 750= Clonidine	☐ 330= Psychiatric Medications (including ADHD and antidepressants)
☐ 110= Coumadin	☐ 340= Statins
☐ 740= Dexmedetomidine	☐ 350= Steroids (oral / IV)
☐ 120= Digoxin	☐ 360= Thyroid Hormone
☐ 130= Direct Thrombin Inhibitors (e.g., argatroban)	☐ 370= Transplant Rejection Inhibition Meds (other than steroids)
☐ 140= Diuretics	☐ 720= Vasoconstrictors Not Otherwise Listed
☐ 150= Dobutamine	☐ 730= Vasodilators Not Otherwise Listed
☐ 160= Dopamine	☐ 380= Vasopressin
☐ 170= Endothelin Antagonist (e.g., Bosentan)	☐ 900= Other
☐ 180= Epinephrine	

Preoperative Sedation ☐ Yes ☐ No

(If Yes→) Preoperative Sedation Route ☐ IM ☐ IV ☐ Nasal ☐ PO (Oral) ☐ Rectal

(If Yes, select all pre-operative sedation drugs that apply: ↓)

Atropine	☐ Yes ☐ No	Ketamine	☐ Yes ☐ No
Demerol	☐ Yes ☐ No	Lorazepam	☐ Yes ☐ No
Dexmedetomidine	☐ Yes ☐ No	Midazolam	☐ Yes ☐ No
Diazepam	☐ Yes ☐ No	Morphine	☐ Yes ☐ No
Fentanyl	☐ Yes ☐ No	Pentobarbital	☐ Yes ☐ No
Glycopyrrolate	☐ Yes ☐ No		

Preoperative Oxygen Saturation: _____ %

Preoperative Oxygen Supplementation ☐ Yes ☐ No

Date and Time of Transport to Procedure Location Or Anesthesia Start Time: *mm/ dd/ yyyy hh : mm* __ __ / __ __ / _ _ _ _ __ __ : __

ANESTHESIA Monitoring

Arterial Line: ☐ Yes ☐ No (If Yes →) Type: (Select all that apply)

Radial	☐ Yes ☐ No	Brachial	☐ Yes ☐ No
Axillary	☐ Yes ☐ No	Femoral	☐ Yes ☐ No
Ulnar	☐ Yes ☐ No	Dorsalis Pedis	☐ Yes ☐ No
Posterior Tibial	☐ Yes ☐ No	Umbilical	☐ Yes ☐ No
Arterial line in-situ pre procedure:	☐ Yes ☐ No		

Cutdown: ☐ Yes ☐ No (If Yes →) Type: (Select all that apply)

Radial	☐ Yes ☐ No	Femoral	☐ Yes ☐ No
Ulnar	☐ Yes ☐ No	Other	☐ Yes ☐ No

Percutaneous Central Pressure: ☐ Yes ☐ No (If Yes →) Location: (Select all that apply)

Right Internal Jugular	☐ Yes ☐ No	Left Internal Jugular	☐ Yes ☐ No
Right Subclavian	☐ Yes ☐ No	Left Subclavian	☐ Yes ☐ No
Right Femoral Vein	☐ Yes ☐ No	Left Femoral Vein	☐ Yes ☐ No
PICC	☐ Yes ☐ No	Other	☐ Yes ☐ No

CVP or PICC in situ pre procedure: ☐ Yes ☐ No

CVP Placed by Anesthesia ☐ Yes ☐ No

Surgeon Placed lines INSTEAD of Anesthesia Placed Central Lines: ☐ Yes ☐ No

Swan-Ganz Catheter ☐ Yes ☐ No

Oximetric Central Line (ScVO2) ☐ Yes ☐ No

Ultrasound Guidance Used for Line Placement: ☐ None ☐ Central venous line ☐ Arterial line ☐ Both arterial & venous lines

Neurologic Monitoring: ☐ Yes ☐ No

(If Yes →)

Bispectral Index	☐ Yes ☐ No
Transcranial Doppler	☐ Yes ☐ No
NIRS (Cerebral)	☐ Yes ☐ No
Other	☐ Yes ☐ No

Lowest Recorded Intraoperative Temperature: _____ °C

Lowest Intraoperative Temperature Site: ☐ Nasal ☐ Esophageal ☐ Bladder ☐ Rectal ☐ Axillary ☐ Skin ☐ Tympanic ☐ Other

Transesophageal Echocardiography ☐ Yes ☐ No

ANESTHESIA Anesthetic Technique

Date and Time of Induction: mm/ dd/ yyyy hh : mm __ __ / __ __ / __ __ __ __ __ __ : __ __

Induction Type:

Inhalation	☐ Yes ☐ No	(If Yes →)	Sevoflurane	☐ Yes ☐ No
			Isoflurane	☐ Yes ☐ No
Intravenous	☐ Yes ☐ No	(If Yes →)	Sodium Thiopental	☐ Yes ☐ No
			Ketamine	☐ Yes ☐ No
			Etomidate	☐ Yes ☐ No
			Propofol	☐ Yes ☐ No
			Fentanyl	☐ Yes ☐ No
			Midazolam	☐ Yes ☐ No
			Dexmedetomidine	☐ Yes ☐ No
			Sufentanil	☐ Yes ☐ No
			Remifentanil	☐ Yes ☐ No
Intramuscular (IM)	☐ Yes ☐ No	(If Yes →)	Ketamine	☐ Yes ☐ No
			Midazolam	☐ Yes ☐ No

Regional Anesthetic ☐ Yes ☐ No

(If Yes →) Regional Anesthetic Site: ☐ Thoracic Epidural Catheter ☐ Lumbar Epidural Catheter ☐ Caudal Epidural Catheter ☐ Lumbar Epidural -Single shot ☐ Caudal Epidural – Single shot ☐ Lumbar Intrathecal -Single Shot ☐ Paravertebral Block-Single shot ☐ Paravertebral Block – Catheter ☐Other

(If Yes →) Regional Anesthetic Drug: *(Select all that apply)*

Bupivicaine	☐ Yes ☐ No	Bupivicaine/Fentanyl	☐ Yes ☐ No
Clonidine	☐ Yes ☐ No	Fentanyl	☐ Yes ☐ No
Hydromorphone	☐ Yes ☐ No	Lidocaine	☐ Yes ☐ No
Morphine	☐ Yes ☐ No	Ropivicaine	☐ Yes ☐ No
Ropivicaine/Fentanyl	☐ Yes ☐ No	Tetracaine	☐ Yes ☐ No
		Other	☐ Yes ☐ No

Intercostal Nerve Infiltration by Surgeon or Anesthesia: ☐ Yes ☐ No

Regional Field Block by Surgeon or Anesthesia: ☐ Yes ☐ No

ANESTHESIA Airway

Airway In-situ (ETT or Tracheostomy): ☐ Yes ☐ No

(If Yes →) ETT or Tracheostomy Replaced for Procedure: ☐ Yes ☐ No

Airway Type: ☐ No airway support ☐ Simple face mask ☐ Bag-mask ☐ Nasal cannulae ☐ Laryngeal Mask Airway (LMA) ☐ Endotracheal intubation ☐ Tracheostomy

(If LMA →) Airway Size *(mm)*: ☐ 1.0 ☐ 1.5 ☐ 2.0 ☐ 2.5 ☐ 3.0 ☐ 4.0 ☐ 5.0

(If Endotracheal intubation →) Airway Size *(mm)*: ☐ 2.5 ☐ 3.0 ☐ 3.5 ☐ 4.0 ☐ 4.5 ☐ 5.0 ☐ 5.5 ☐ 6.0 ☐ 6.5 ☐ 7.0 ☐ 7.5 ☐ 8.0 ☐ Other ☐ Size not listed (DLETT, Tracheotomy)

Cuffed ☐ Yes ☐ No

(If Endotracheal intubation or Trach→) Airway Site: ☐ Oral ☐ Nasal ☐ Tracheostomy

Endobronchial Isolation (DLETT, Bronchial Blocker) ☐ Yes ☐ No

(If Yes →) Endobronchial Isolation Method: ☐ Double lumen ETT ☐ Arndt Bronchial Blocker ☐ Fogarty Catheter ☐ Intentional Mainstem ETT ☐ Uninvent ETT ☐ Other

ICU Type Ventilator Used Intraop: ☐ Yes ☐ No

Anesthesia Ready / End of Induction: *mm/ dd/ yyyy hh : mm* __ /__ /_____ __:__

ANESTHESIA Intraoperative Pharmacology (including CPB)

Intraoperative Medications: ☐ None *(If not None, select all intra-operative medications that apply: ↓)*

☐ 450= 5-HT3 Agents (e.g., Ondansetron)	☐ 190= Magnesium Sulfate
☐ 520= Acetaminophen	☐ 210= Milrinone
☐ 20= Adenosine bolus	☐ 430= Narcotic
☐ 50= Amiodarone	☐ 230= Nesiritide Infusion
☐ 440= Benzodiazepine	☐ 240= Nicardipine Infusion
☐ 420= Bronchodilator - Inhaled	☐ 250= Nitric Oxide inhalation
☐ 70= Calcium Chloride infusion	☐ 260= Nitroglycerin (Tridil) infusion
☐ 75= Calcium Gluconate infusion	☐ 270= Nitroprusside (Nipride)
☐ 480= Desflurane	☐ 180= Norepinephrine (Levophed) infusion
☐ 80= Dexmetetomidine (Precedex)	☐ 280= Phenoxybenzamine bolus
☐ 90= Dobutamine infusion	☐ 290= Phentolamine (Regitine)
☐ 100= Dopamine infusion	☐ 300= Phenylephrine infusion
☐ 110= Epinephrine (Adrenalin) infusion	☐ 500= Procainamide
☐ 120= Esmolol	☐ 310= Propofol (Diprivan) infusion
☐ 510= Fenoldopam infusion	☐ 320= Prostaglandin infusion
☐ 140= Furosemide	☐ 470= Sevoflurane
☐ 370= Inotrope, Other	☐ 400= Sodium Bicarbonate bolus
☐ 150= Insulin	☐ 160= Steroids IV/CPB (Hydrocortisone/Methylprednisolone/Dexamethasone)
☐ 460= Isoflurane	☐ 340= Thyroid Hormone

☐ 170= Isoproterenol infusion	☐ 410= Tromethamine (THAM) bolus
☐ 490= Ketamine	☐ 390= Vasoconstrictor, Other
☐ 530= Ketorolac	☐ 380= Vasodilator, Other
☐ 540= Levosimendan	☐ 360= Vasopressin infusion

ANESTHESIA Pharmacology On Arrival To ICU/PACU

Medications Given At Time Of Transfer: ☐ None *(If not None, select all medications that apply: ↓)*

☐ 20= Aminocaproic Acid (Amicar) infusion	☐ 170= Muscle Relaxant infusion
☐ 30= Amiodarone infusion	☐ 360= Narcotic infusion
☐ 40= Aprotinin (Trasylol) infusion	☐ 180= Nesiritide Infusion
☐ 370= Benzodiazepine infusion	☐ 190= Nicardipine infusion
☐ 50= Calcium Chloride infusion	☐ 200= Nitric Oxide inhalation
☐ 60= Calcium Gluconate infusion	☐ 210= Nitroglycerin (Tridil) infusion
☐ 70= Dexmetetomidine (Precedex) infusion	☐ 220= Nitroprusside (Nipride) infusion
☐ 80= Dobutamine infusion	☐ 230= Norepinephrine (Levophed) infusion
☐ 90= Dopamine infusion	☐ 240= Phentolamine (Regitine) infusion
☐ 100= Epinephrine (Adrenalin) infusion	☐ 250= Phenylephrine infusion
☐ 340= Esmolol infusion	☐ 380= Procainamide bolus/infusion
☐ 390= Fenoldopam infusion	☐ 260= Propofol (Diprivan) infusion
☐ 310= Inotrope, Other	☐ 270= Prostaglandin infusion
☐ 120=Insulin infusion	☐ 280= Thyroid Hormone infusion
☐ 130= Isoproterenol infusion	☐ 290= Tranexamic Acid infusion
☐ 400= Levosimendan	☐ 330= Vasoconstrictor, Other
☐ 350= Local Anesthetic infusion via catheter (On-Q, Pleural catheter)	☐ 320= Vasodilator, Other
☐ 150= Milrinone infusion	☐ 300= Vasopressin infusion

ANESTHESIA ICU/PACU Care

Date and Time of ICU/PACU Arrival: *(mm/dd/yyyy 00:00 – 23:59)* _ _ / _ _ / _ _ _ _ _ _:_ _

Initial FiO2:_____ | Mechanical circulatory support(ECMO/VAD) : ☐ Yes ☐ No

ICU/PACU Arrival labs ☐ Yes ☐ No *(If Yes →)* pH: ____ pCO2: ____ pO2: ____
Base Excess: ____ Lactate: ____ Hematocrit: ____

Initial pulse oximeter _____ % Temperature on ICU/PACU Arrival: _____ ° C

Temperature Measurement Site: ☐ Forehead scan ☐ Tympanic membrane ☐ Skin ☐ Rectal ☐ Bladder ☐ Oral ☐ Axillary ☐ Other

Need for Temporary Pacemaker on Arrival In ICU/PACU: ☐ Yes ☐ No

(If Yes →) Site of Temporary Pace Maker: ☐ Epicardial ☐ Transvenous

(If Yes →) Type of Temporary Pacing: ☐ Atrial ☐ Atrio-ventricular ☐ Ventricular ☐ Other

Disposition Under Anesthesia: ☐ Discharged as planned after PACU/Recovery ☐ Admit to hospital floor as planned ☐ Admit to ICU as planned ☐ Unplanned admit to hospital or ICU ☐ Other location not listed above ☐ Patient expired under anesthetic management

Peri-Anesthetic Demise: (within 24 hr of last anesthetic end time) ☐ Yes ☐ No

ANESTHESIA Adverse Events

If Anesthesia Adverse Event is not 'None' or missing:
Additional Intervention Required:
Circle EACH event that required additional intervention.

Anesthesia adverse events: ☐ None *(If not None, select all adverse events that apply: ↓)*

☐ 20= Oral/Nasal Injury-Bleeding	☐ 210= Anaphylaxis/Anaphylactoid Reaction
☐ 30= Respiratory Arrest	☐ 220= Non-allergic Drug Reaction
☐ 40= Difficult Intubation/Reintubation	☐ 230= Medication Administration
☐ 50= Stridor / Sub-glottic Stenosis	☐ 240= Medication Dosage
☐ 60= Extubation	☐ 250= Intraoperative Recall

☐ 70= Endotracheal Tube Migration	☐ 260= Malignant Hyperthermia
☐ 80= Airway Injury	☐ 270= Protamine Reaction
☐ 410= Hemoptysis	☐ 280= Cardiac Arrest - related to anesthesia care
☐ 450= Laryngospasm requiring medication	☐ 490= Cardiac Arrest - unrelated to anesthesia care
☐ 400= Bronchospasm	☐ 510= Hypercyanotic Episode (Tet Spell) unrelated to manipulation
☐ 470= Unplanned need to remain intubated post-procedure due to anesthesia factors	☐ 500= Pulmonary Hypertensive Crisis unrelated to manipulation
☐ 90= Arrhythmia - Central Venous Line Placement	☐ 290= TEE related esophageal bleeding / rupture
☐ 100= Myocardial Injury - Central Venous Line Placement	☐ 300= TEE related esophageal chemical burn
☐ 110= Vascular Compromise - Central Venous Line Placement	☐ 310= TEE related airway compromise
☐ 120= Pneumothorax - Central Venous Line Placement	☐ 315= TEE related hemodynamic compromise
☐ 130= Vascular Access	☐ 320= TEE related extubation
☐ 140= Hematoma requiring relocation of catheter placement	☐ 330= Complications during patient transfer
☐ 150= Arterial Puncture	☐ 340= Peripheral Nerve Injury due to positioning
☐ 160= Intravenous/Intra-arterial Air Embolism	☐ 370= Anesthesia Equipment Malfunction/ Failure
☐ 350= Arterial Line Placement- Extremity ischemia	☐ 390= Integument Injury (skin breakdown or dehiscence)
☐ 380= Intravenous Infiltration	☐ 480= Ocular Injury (corneal abrasion or injury)
☐ 170= Bleeding - Regional Anesthetic Site	☐ 420= Postop Nausea/Vomiting requiring admission
☐ 180= Intrathecal Puncture - Regional	☐ 430= Vomiting or Aspiration on Induction/Emergence
☐ 190= Local Anesthetic Toxicity - Regional	☐ 440= Emergence Delirium requiring Medication
☐ 200= Neurologic Injury - Regional	☐ 900= Other

15.2 Appendix A2: Data element definitions for the STS-CHSD

STS Congenital Heart Surgery Database Data Specifications

Version 3.3

This document current as of: 6/26/2015 4:01:13 PM

This document contains information specific for vendors and software developers

Note: **- ALL fields defined in these specifications with "Core: Yes" are to be collected by all sites.**

- A data record must be created for each time the patient enters the Operating Room.

- Fields indicated with a gray background are no longer being collected.

STS Congenital Heart Surgery Database — Version 3.3

Long Name:	Participant ID	*SeqNo:*	10
Short Name:	**ParticID**	*Core:*	Yes
Section Name:	Administrative	*Harvest:*	Yes
DBTableName	Operations	*DataLength:*	5
		Field Status:	Continued

Definition: Participant ID is a unique number assigned to each database participant by the STS. A database participant is defined as one entity that signs a Participation Agreement with the STS, submits one data file to the harvest, and gets back one report on their data. The participant ID must be entered into each record.
Each participant's data, if submitted to harvest, must be in one data file. If one participant keeps their data in more than one file (e.g., at two sites), then the participant must combine them back into one file for harvest submission.
If two or more participants share a single purchased software, and enter cases into one database, then the data must be extracted into two different files, one for each participant ID, with each record having the correct participant ID number.

Data Source: User or Automatic *Format* Text

Long Name:	STS Data Version	*SeqNo:*	20
Short Name:	**DataVrsn**	*Core:*	Yes
Section Name:	Administrative	*Harvest:*	Yes
DBTableName	Operations	*DataLength:*	8
		Field Status:	Continued

Definition: Version number of the STS Data Specifications/Dictionary, to which each record conforms. It will identify which fields should have data, and what are the valid data for each field. This must be entered into the record automatically by the software at the time the record is created.

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15.3 Appendix B: Package insert for intravenous methylprednisolone

SOLU-MEDROL® (methylprednisolone sodium succinate for injection, USP)

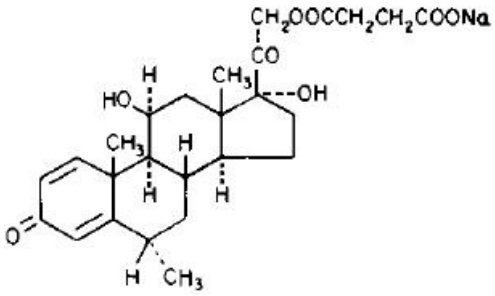
The formulations containing benzyl alcohol should not be used in neonates.

For Intravenous or Intramuscular Administration

DESCRIPTION

SOLU-MEDROL Sterile Powder is an anti-inflammatory glucocorticoid, which contains methylprednisolone sodium succinate as the active ingredient. Methylprednisolone sodium succinate, USP, is the sodium succinate ester of methylprednisolone, and it occurs as a white, or nearly white, odorless hygroscopic, amorphous solid. It is very soluble in water and in alcohol; it is insoluble in chloroform and is very slightly soluble in acetone.

The chemical name for methylprednisolone sodium succinate is pregna-1,4-diene-3,20dione,21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-monosodium salt, (6α, 11β), and the molecular weight is 496.53. The structural formula is represented below:



Methylprednisolone sodium succinate is soluble in water; it may be administered in a small volume of diluent and is well suited for intravenous use in situations where high blood levels of methylprednisolone are required rapidly.

SOLU-MEDROL is available in preservative and preservative-free formulations: **Preservative-free Formulations**
40 mg Act-O-Vial System (Single-Use Vial)—Each mL (when mixed) contains methylprednisolone sodium succinate equivalent to 40 mg methylprednisolone; also 1.6 mg monobasic sodium phosphate anhydrous; 17.46 mg dibasic sodium phosphate dried; and 25 mg lactose hydrous.
125 mg Act-O-Vial System (SingleUse Vial)—Each 2 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 125 mg methylprednisolone; also 1.6 mg monobasic sodium phosphate anhydrous; and 17.4 mg dibasic sodium phosphate dried.

500 mg Act-O-Vial System (SingleUse Vial)—Each 4 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone; also 6.4 mg monobasic sodium phosphate anhydrous; and 69.6 mg dibasic sodium phosphate dried.
1 gram Act-O-Vial System (SingleUse Vial)—Each 8 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 1 gram methylprednisolone; also 12.8 mg monobasic sodium phosphate anhydrous; and 139.2 mg dibasic sodium phosphate dried.

Formulations preserved with Benzyl Alcohol
40 mg Act-O-Vial System (Single-Use Vial)—Each mL (when mixed) contains methylprednisolone sodium succinate equivalent to 40 mg methylprednisolone; also 1.6 mg monobasic sodium phosphate anhydrous; 17.46 mg dibasic sodium phosphate dried; 25 mg lactose hydrous; 8.8 mg benzyl alcohol added as preservative.
125 mg Act-O-Vial System (Single-Use Vial)—Each 2 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 125 mg methylprednisolone; also 1.6 mg monobasic sodium phosphate anhydrous; 17.4 mg dibasic sodium phosphate dried; 17.6 mg benzyl alcohol added as preservative.
500 mg Act-O-Vial System (Single-Use Vial)—Each 4 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone; also 6.4 mg monobasic sodium phosphate anhydrous; 69.6 mg dibasic sodium phosphate dried; 33.7 mg benzyl alcohol added as preservative.
1 gram Act-O-Vial System (Single-Use Vial)—Each 8 mL (when mixed) contains methylprednisolone sodium succinate equivalent to 1 gram methylprednisolone; also 12.8 mg monobasic sodium phosphate anhydrous; 139.2 mg dibasic sodium phosphate dried; 66.8 mg benzyl alcohol added as preservative.
500 mg Vial—Each 8 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 500 mg methylprednisolone; also 6.4 mg monobasic sodium phosphate anhydrous; 69.6 mg dibasic sodium phosphate dried. This package does not contain diluent. Recommended diluent (Bacteriostatic water) contains benzyl alcohol as a preservative.
1 gram Vial—Each 16 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 1 gram methylprednisolone; also 12.8 mg monobasic sodium phosphate anhydrous; 139.2 mg dibasic sodium phosphate dried. This package does not contain diluent. Recommended diluent (Bacteriostatic water) contains benzyl alcohol as a preservative.
2 gram Vial with Diluent—Each 30.6 mL (when mixed as directed) contains methylprednisolone sodium succinate equivalent to 2 grams methylprednisolone; also 25.6 mg monobasic sodium phosphate anhydrous; 278 mg dibasic sodium phosphate dried; 273 mg benzyl alcohol added as preservative. The packaged diluent (Bacteriostatic Water for Injection) contains benzyl alcohol as a preservative.
IMPORTANT — Use only the accompanying diluent or Bacteriostatic Water For Injection with Benzyl Alcohol when reconstituting SOLU-MEDROL. **Use within 48 hours after mixing.**

When necessary, the pH of each formula was adjusted with sodium hydroxide so that the pH of the reconstituted solution is within the USP specified range of 7 to 8 and the tonicities are, for the 40 mg per mL solution, 0.50 osmolar; for the 125 mg per 2 mL solution, 0.40 osmolar; for the 1 gram

per 8 mL solution, 0.44 osmolar; for the 2 gram per 30.6 mL solutions, 0.42 osmolar. (Isotonic saline = 0.28 osmolar.)

CLINICAL PHARMACOLOGY

Glucocorticoids, naturally occurring and synthetic, are adrenocortical steroids that are readily absorbed from the gastrointestinal tract.

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

Methylprednisolone is a potent anti-inflammatory steroid with greater anti-inflammatory potency than prednisolone and even less tendency than prednisolone to induce sodium and water retention.

Methylprednisolone sodium succinate has the same metabolic and anti-inflammatory actions as methylprednisolone. When given parenterally and in equimolar quantities, the two compounds are equivalent in biologic activity. Following the intravenous injection of methylprednisolone sodium succinate, demonstrable effects are evident within one hour and persist for a variable period. Excretion of the administered dose is nearly complete within 12 hours. Thus, if constantly high blood levels are required, injections should be made every 4 to 6 hours. This preparation is also rapidly absorbed when administered intramuscularly and is excreted in a pattern similar to that observed after intravenous injection.

INDICATIONS AND USAGE

When oral therapy is not feasible, and the strength, dosage form, and route of administration of the drug reasonably lend the preparation to the treatment of the condition, the **intravenous or intramuscular use** of SOLU-MEDROL Sterile Powder is indicated as follows:

Allergic states: Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in asthma, atopic dermatitis, contact dermatitis, drug hypersensitivity reactions, perennial or seasonal allergic rhinitis, serum sickness, transfusion reactions.

Dermatologic diseases: Bullous dermatitis herpetiformis, exfoliative erythroderma, mycosis fungoides, pemphigus, severe erythema multiforme (Stevens-Johnson syndrome).

Endocrine disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular

importance), congenital adrenal hyperplasia, hypercalcemia associated with cancer, nonsuppurative thyroiditis.

Gastrointestinal diseases: To tide the patient over a critical period of the disease in regional enteritis (systemic therapy) and ulcerative colitis.

Hematologic disorders: Acquired (autoimmune) hemolytic anemia, congenital (erythroid) hypoplastic anemia (Diamond-Blackfan anemia), idiopathic thrombocytopenic purpura in adults (intravenous administration only; intramuscular administration is contraindicated), pure red cell aplasia, selected cases of secondary thrombocytopenia.

Miscellaneous: Trichinosis with neurologic or myocardial involvement, tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.

Neoplastic diseases: For the palliative management of leukemias and lymphomas.

Nervous System: Acute exacerbations of multiple sclerosis; cerebral edema associated with primary or metastatic brain tumor, or craniotomy.

Ophthalmic diseases: Sympathetic ophthalmia, uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids.

Renal diseases: To induce diuresis or remission of proteinuria in idiopathic nephrotic syndrome or that due to lupus erythematosus.

Respiratory diseases: Berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy, idiopathic eosinophilic pneumonias, symptomatic sarcoidosis.

Rheumatic disorders: As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in acute gouty arthritis; acute rheumatic carditis; ankylosing spondylitis; psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy). For the treatment of dermatomyositis, temporal arteritis, polymyositis, and systemic lupus erythematosus.

CONTRAINDICATIONS

SOLU-MEDROL Sterile Powder is contraindicated:

- in systemic fungal infections and patients with known hypersensitivity to the product and its constituents.
- for intrathecal administration. Reports of severe medical events have been associated with this route of administration.

Intramuscular corticosteroid preparations are contraindicated for idiopathic thrombocytopenic purpura.

Additional contraindication for the use of SOLU-MEDROL Sterile Powder preserved with benzyl alcohol:
Formulations preserved with benzyl alcohol are contraindicated for use in premature infants. (See **WARNINGS** and **PRECAUTIONS**, **Pediatric Use**.

WARNINGS

Serious Neurologic Adverse Reactions with Epidural Administration
Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy. The safety and effectiveness of epidural administration of corticosteroids have not been established, and corticosteroids are not approved for this use.

GENERAL
Formulations with preservative (see DESCRIPTION) contain benzyl alcohol, which is potentially toxic when administered locally to neural tissue. Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates, and an increased incidence of kernicterus, particularly in small preterm infants. There have been rare reports of deaths, primarily in preterm infants, associated with exposure to excessive amounts of benzyl alcohol. The amount of benzyl alcohol from medications is usually considered negligible compared to that received in flush solutions containing benzyl alcohol. Administration of high dosages of medications containing this preservative must take into account the total amount of benzyl alcohol administered. The amount of benzyl alcohol at which toxicity may occur is not known. If the patient requires more than the recommended dosages or other medications containing this preservative, the practitioner must consider the daily metabolic load of benzyl alcohol from these combined sources (see **PRECAUTIONS**, **Pediatric Use**).

Injection of SOLU-MEDROL may result in dermal and/or subdermal changes forming depressions in the skin at the injection site. In order to minimize the incidence of dermal and subdermal atrophy, care must be exercised not to exceed recommended doses in injections. Injection into the deltoid muscle should be avoided because of a high incidence of subcutaneous atrophy.

Rare instances of anaphylactoid reactions have occurred in patients receiving corticosteroid therapy (see **ADVERSE REACTIONS**).

Increased dosage of rapidly acting corticosteroids is indicated in patients on corticosteroid therapy who are subjected to any unusual stress before, during, and after the stressful situation.

Results from one multicenter, randomized, placebo-controlled study with methylprednisolone hemisuccinate, an intravenous corticosteroid, showed an increase in early (at 2 weeks) and late

(at 6 months) mortality in patients with cranial trauma who were determined not to have other clear indications for corticosteroid treatment. High doses of systemic corticosteroids, including SOLU-MEDROL, should not be used for the treatment of traumatic brain injury.

Cardio-renal
Average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Literature reports suggest an apparent association between the use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction; therefore, therapy with corticosteroids should be used with great caution in these patients.

Endocrine
Hypothalamic-pituitary adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia. Monitor patients for these conditions with chronic use.

Corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Drug induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted.

Drug-Induced Liver Injury
Rarely, high doses of cyclically pulsed intravenous methylprednisolone (usually for the treatment of exacerbations of multiple sclerosis at doses of 1 gram/day) can induce a toxic form of acute hepatitis. The time to onset of this form of steroid-induced liver injury can be several weeks or longer. Resolution has been observed after discontinuation of treatment. However, serious liver injury can occur, sometimes resulting in acute liver failure and death. Discontinue intravenous methylprednisolone if toxic hepatitis occurs. Since recurrence has occurred after re-challenge, avoid use of high dose intravenous

methylprednisolone in patients with a history of toxic hepatitis caused by methylprednisolone.

Infections
General
Patients who are on corticosteroids are more susceptible to infections than are healthy individuals. There may be decreased resistance and inability to localize infection when corticosteroids are used. Infections with any pathogen (viral, bacterial, fungal, protozoan, or helminthic) in any location of the body may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents.

These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases. Corticosteroids may also mask some signs of current infection. Do not use intraarticularly, intrabursally or for intratendinous administration for local effect in the presence of acute local infection.

A study has failed to establish the efficacy of methylprednisolone sodium succinate in the treatment of sepsis syndrome and septic shock. The study also suggests that treatment of these conditions with methylprednisolone sodium succinate may increase the risk of mortality in certain patients (i.e., patients with elevated serum creatinine levels or patients who develop secondary infections after methylprednisolone sodium succinate).

Fungal infections
Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure (see **CONTRAINDICATIONS** and **PRECAUTIONS**, **Drug Interactions**, *Amphotericin B injection and potassium-depleting agents*).

Special pathogens
Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by *Amoeba, Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis, Toxoplasma*.

It is recommended that latent amebiasis or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Similarly, corticosteroids should be used with great care in patients with known or suspected *Strongyloides* (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to *Strongyloides* hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria. There is currently no evidence of benefit from steroids in this condition.

Tuberculosis
The use of corticosteroids in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Vaccination

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered. However, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Viral infections
Chicken pox and measles can have a more serious or even fatal course in pediatric and adult patients on corticosteroids. In pediatric and adult patients who have not had these diseases, particular care should be taken to avoid exposure. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chicken pox develops, treatment with antiviral agents should be considered.

Neurologic
Reports of severe medical events have been associated with the intrathecal route of administration (see **ADVERSE REACTIONS**, *Gastrointestinal* and *Neurologic/Psychiatric*).

Ophthalmic
Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of corneal perforation. Corticosteroids should not be used in active ocular herpes simplex.

PRECAUTIONS

General
This product, like many other steroid formulations, is sensitive to heat. Therefore, it should not be autoclaved when it is desirable to sterilize the exterior of the vial.

The lowest possible dose of corticosteroid should be used to control the condition under treatment. When reduction in dosage is possible, the reduction should be gradual.

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Cardio-renal

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with congestive heart failure, hypertension, or renal insufficiency.

Endocrine
Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted.

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Gastrointestinal
Steroids should be used with caution in active or latent peptic ulcers, diverticulitis, fresh intestinal anastomoses, and nonspecific ulcerative colitis, since they may increase the risk of a perforation. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent.

There is an enhanced effect due to decreased metabolism of corticosteroids in patients with cirrhosis.

Musculoskeletal
Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e., decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in pediatric patients and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy.

Local injection of a steroid into a previously infected site is not usually recommended.

Neurologic-Psychiatric
Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that corticosteroids affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See **DOSAGE AND ADMINISTRATION**.)

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory

muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Ophthalmic
Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.

Information for Patients
Patients should be warned not to discontinue the use of corticosteroids abruptly or without medical supervision, to advise any medical attendants that they are taking corticosteroids, and to seek medical advice at once should they develop fever or other signs of infection.

Persons who are on corticosteroids should be warned to avoid exposure to chicken pox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Drug Interactions
Aminoglutethimide: Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.
Amphotericin B injection and potassium-depleting agents: When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., amphotericin B, diuretics), patients should be observed closely for development of hypokalemia. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.

Antibiotics: Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance (see **Drug Interactions**, *Hepatic Enzyme Inhibitors*).

Anticholinesterases: Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Anticoagulants, oral: Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

Antidiabetics: Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.

Antitubercular drugs: Serum concentrations of isoniazid may be decreased.

Cholestyramine: Cholestyramine may increase the clearance of corticosteroids.

Cyclosporine: Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Digitalis glycosides: Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.

Estrogens, including oral contraceptives: Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.

Hepatic Enzyme Inducers (e.g., barbiturates, phenytoin, carbamazepine, rifampin): Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.

Hepatic Enzyme Inhibitors (e.g., ketoconazole, macrolide antibiotics such as erythromycin and troleandomycin): Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids.

Ketoconazole: Ketoconazole has been reported to significantly decrease the metabolism of certain corticosteroids by up to 60%, leading to an increased risk of corticosteroid side effects.

Nonsteroidal anti-inflammatory agents (NSAIDs): Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

Skin tests: Corticosteroids may suppress reactions to skin tests.

Vaccines: Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible (see **WARNINGS**, **Infections**, ***Vaccination***).

Carcinogenesis, Mutagenesis, Impairment of Fertility
No adequate studies have been conducted in animals to determine whether corticosteroids have a potential for carcinogenesis or mutagenesis.

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Corticosteroids have been shown to impair fertility in male rats.

Pregnancy: Teratogenic effects: Pregnancy Category C.

Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well-controlled studies in pregnant women. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

This product contains benzyl alcohol as a preservative. Benzyl alcohol can cross the placenta. See **PRECAUTIONS: Pediatric use**.

Nursing Mothers
Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Because of the potential for serious adverse reactions in nursing infants from corticosteroids, a decision should be made whether to continue nursing, or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Some formulations of this product contain benzyl alcohol as a preservative (see DESCRIPTION). Carefully examine vials to determine formulation that is being used.

Benzyl alcohol, a component of this product, has been associated with serious adverse events and death, particularly in pediatric patients. The “gasping syndrome” (characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates and low-birth-weight neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Although normal therapeutic doses of this product ordinarily delivers amounts of benzyl alcohol that are substantially lower than those reported in association with the “gasping syndrome”, the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the hepatic capacity to detoxify the chemical. Premature and low-birth-weight infants, as well as patients receiving high dosages, may be more likely to develop toxicity. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

The efficacy and safety of corticosteroids in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (>2 years of age), and aggressive lymphomas and leukemias (>1 month of age). Other indications for pediatric use of corticosteroids, e.g., severe asthma and wheezing, are based on adequate and well- controlled trials conducted in adults, on

the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations.

The adverse effects of corticosteroids in pediatric patients are similar to those in adults (see **ADVERSE REACTIONS**). Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Pediatric patients who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The linear growth of pediatric patients treated with corticosteroids should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of treatment alternatives. In order to minimize the potential growth effects of corticosteroids, pediatric patients should be titrated to the lowest effective dose.

Geriatric Use
Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

The following adverse reactions have been reported with SOLU-MEDROL or other corticosteroids:

Allergic reactions: Allergic or hypersensitivity reactions, anaphylactoid reaction, anaphylaxis, angioedema.

Blood and lymphatic system disorders: Leukocytosis.

Cardiovascular: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction (see **WARNINGS**), pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis.

Dermatologic: Acne, allergic dermatitis, burning or tingling (especially in the perineal area after intravenous injection), cutaneous and subcutaneous atrophy, dry scaly skin, ecchymoses and

petechiae, edema, erythema, hyperpigmentation, hypopigmentation, impaired wound healing, increased sweating, rash, sterile abscess, striae, suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria.

Endocrine: Decreased carbohydrate and glucose tolerance, development of cushingoid state, glycosuria, hirsutism, hypertrichosis, increased requirements for insulin or oral hypoglycemic agents in diabetes, manifestations of latent diabetes mellitus, menstrual irregularities, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), suppression of growth in pediatric patients.

Fluid and electrolyte disturbances: Congestive heart failure in susceptible patients, fluid retention, hypokalemic alkalosis, potassium loss, sodium retention.

Gastrointestinal: Abdominal distention, bowel/bladder dysfunction (after intrathecal administration), elevation in serum liver enzyme levels (usually reversible upon discontinuation), hepatomegaly, increased appetite, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), ulcerative esophagitis.

Hepatobiliary: Hepatitis (see **WARNINGS**, **Drug-Induced Liver Injury**).

Metabolic: Negative nitrogen balance due to protein catabolism.

Musculoskeletal: Aseptic necrosis of femoral and humeral heads, Charcot-like arthropathy, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, postinjection flare (following intra-articular use), steroid myopathy, tendon rupture, vertebral compression fractures.

Neurologic/Psychiatric: Convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudotumor cerebri) usually following discontinuation of treatment, insomnia, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo. Arachnoiditis, meningitis, paraparesis/paraplegia, and sensory disturbances have occurred after intrathecal administration (see **WARNINGS**, **Neurologic**).

Ophthalmic: Exophthalmos, glaucoma, increased intraocular pressure, posterior subcapsular cataracts, rare instances of blindness associated with periocular injections.

Other: Abnormal fat deposits, decreased resistance to infection, hiccups, increased or decreased motility and number of spermatozoa, injection site infections following non- sterile administration (see **WARNINGS**), malaise, moon face, weight gain.

OVERDOSAGE

Treatment of acute overdosage is by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy, the dosage of the corticosteroid may be reduced only temporarily, or alternate day treatment may be introduced.

DOSAGE AND ADMINISTRATION

NOTE: Some of the SOLU-MEDROL formulations contain benzyl alcohol (see DESCRIPTION, WARNINGS and PRECAUTIONS, Pediatric Use)

Because of possible physical incompatibilities, SOLU-MEDROL should not be diluted or mixed with other solutions.

Use only the accompanying diluent or Bacteriostatic Water For Injection with Benzyl Alcohol when reconstituting SOLU-MEDROL (see DESCRIPTION). Use within 48 hours after mixing.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

This preparation may be administered by intravenous injection, by intravenous infusion, or by intramuscular injection, the preferred method for initial emergency use being intravenous injection. Following the initial emergency period, consideration should be given to employing a longer acting injectable preparation or an oral preparation.

There are reports of cardiac arrhythmias and/or cardiac arrest following the rapid administration of large intravenous doses of SOLU-MEDROL (**greater than 0.5 gram administered over a period of less than 10 minutes**). Bradycardia has been reported during or after the administration of large doses of methylprednisolone sodium succinate, and may be unrelated to the speed or duration of infusion. When high dose therapy is desired, the recommended dose of SOLU-MEDROL Sterile Powder is 30 mg/kg **administered intravenously over at least 30 minutes**. This dose may be repeated every 4 to 6 hours for 48 hours.

In general, high dose corticosteroid therapy should be continued only until the patient's condition has stabilized; usually not beyond 48 to 72 hours.

In other indications, initial dosage will vary from 10 to 40 mg of methylprednisolone depending on the specific disease entity being treated. However, in certain overwhelming, acute, life-threatening situations, administrations in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages. *It Should Be Emphasized that Dosage Requirements are Variable and Must Be Individualized on the Basis of the Disease Under Treatment and the Response of the Patient.* After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. Situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment. In this latter situation, it may be necessary to increase the dosage of the corticosteroid for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

SOLU-MEDROL may be administered by intravenous or intramuscular injection or by intravenous infusion, the preferred method for initial emergency use being intravenous injection. To administer by intravenous (or intramuscular) injection, prepare solution as directed. The desired dose may be administered intravenously over a period of several minutes. If desired, the medication may be administered in diluted solutions by adding Water for Injection or other suitable diluent (see below) to the **Act-O-Vial** and withdrawing the indicated dose.

To prepare solutions for intravenous infusion, first prepare the solution for injection as directed. This solution may then be added to indicated amounts of 5% dextrose in water, isotonic saline solution, or 5% dextrose in isotonic saline solution.

In pediatric patients, the initial dose of methylprednisolone may vary depending on the specific disease entity being treated. The range of initial doses is 0.11 to 1.6 mg/kg/day in three or four divided doses (3.2 to 48 mg/m^2bsa/day).

The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic *prednisone, prednisolone, or methylprednisolone* in pediatric patients whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued until the patient achieves a peak expiratory flow rate of 80% of his or her personal best or until symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse.

Dosage may be reduced for infants and children but should be governed more by the severity of the condition and response of the patient than by age or size. It should not be less than 0.5 mg per kg every 24 hours.

Dosage must be decreased or discontinued gradually when the drug has been administered for more than a few days. If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued. Routine laboratory studies, such as urinalysis, two-hour postprandial blood sugar, determination of blood pressure and body weight, and a chest X-ray should be made at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with an ulcer history or significant dyspepsia.

In treatment of acute exacerbations of multiple sclerosis, daily doses of 160 mg of methylprednisolone for a week followed by 64 mg every other day for 1 month have been shown to be effective (see **PRECAUTIONS**, **Neurologic-psychiatric**).

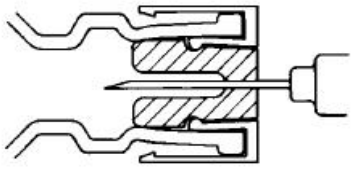
For the purpose of comparison, the following is the equivalent milligram dosage of the various glucocorticoids:

Cortisone, 25	Triamcinolone, 4
Hydrocortisone, 20	Paramethasone, 2
Prednisolone, 5	Betamethasone, 0.75
Prednisone, 5	Dexamethasone, 0.75
Methylprednisolone, 4	

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

DIRECTIONS FOR USING THE ACT-O-VIAL SYSTEM

1. Press down on plastic activator to force diluent into the lower compartment.
2. Gently agitate to effect solution.
3. Remove plastic tab covering center of stopper.
4. Sterilize top of stopper with a suitable germicide.
5. Insert needle **squarely through center** of stopper until tip is just visible. Invert vial and withdraw dose.



STORAGE CONDITIONS

Protect from light.

Store unreconstituted product at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

Store solution at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

Use solution within 48 hours after mixing.

HOW SUPPLIED

SOLU-MEDROL Sterile Powder preserved with benzyl alcohol is available in the following packages:

500 mg (Multi-Dose Vial)
8 mL NDC 0009-0758-01

1 gram (Multi-Dose Vial)
16 mL NDC 0009-0698-01

2 gram Vial with Diluent
NDC 0009-0796-01

SOLU-MEDROL Sterile Powder **preservative-free** is available in the following packages:

40 mg Act-O-Vial System (Single-Use Vial) Vial)
25 x1 mL NDC 0009-0039-28

125 mg Act-O-Vial System (Single-Use Vial)
25 x 2 mL NDC 0009-0047-22

500 mg Act-O-Vial System (Single-Use Vial)
4 mL NDC 0009-0003-02

1 gram Act-O-Vial System (Single-Use Vial)
8 mL NDC 0009-0018-20

Pfizer Injectables

Distributed by
Pharmacia & Upjohn Co
Division of Pfizer Inc
New York, NY 10017

LAB-0161-8.2 Revised July 2016

15.4 Appendix C: Plasma PK sampling and handling

Timing of samples will treat the time of initial drug administration as time (0). The date and time will be recorded for the time of drug administration and for the acquisition time of the PK sample. The PK/PD/Biomarker samples will be obtained in sodium heparin collection tubes.

1. For the scheduled pharmacokinetic draws, one 800uL blood sample will be collected from a peripheral IV or central line site into the provided sodium heparin tubes, and placed on ice.
2. Immediately, within one-half hour of the blood draw, centrifuge at 3,500 g for 5 minutes at approximately 4°C.
3. Transfer plasma into the provided polypropylene screw cap transfer tubes.
4. Transfer tubes should be labeled with a pre-printed label containing site, patient number, and protocol collection time. Ensure that the pre-printed label corresponds to the recorded date and time of collection on the CRF.
5. Immediately freeze the specimens (-70°C) in an upright position. Notify the Protocol Chair immediately if the samples become thawed or damaged.
6. Ship frozen at times specified, to the designated specialty laboratory.

15.5 Appendix D: Protocol Amendments

Amendment #	Date	Change
#1	02 September 2017	Changes the dosing regimen from a two dose regimen including pre-operative + intraoperative methylprednisolone (30mg/kg/dose)/placebo, to a single dose regimen consisting of only intra-operative methylprednisolone (30mg/kg)/placebo.
#2	29 June 2018	Expands the inclusion criteria from neonates < 30 days of age at time of heart surgery with cardiopulmonary bypass (CPB) to infants < 1 year of age undergoing surgery.
#3	16 October 2018	Removes Digoxin from the list of medications that would exclude a patient if they have been taken within 2 days of the cardiopulmonary bypass (CPB) surgery
#4	15 September 2020	Correctly defines neonate as age ≤30 days to be consistent with SAS code in the STS-CHSD database and updates plan for the interim analysis.
#5	27 March 2022	Amends protocol to note we will follow study participants for a minimum of 4 months from date of surgery (changed from 6 months). The rationale for the change is patients remain hospitalized at the end of the study, and to complete the study statistical analysis before the end of the project period, we need to limit the duration of follow up to 4 months. Also amends protocol to assign a worst outcome of heart transplant to subjects hospitalized, listed for transplant and receiving mechanical support. The rationale for this is that heart transplant is the second worst outcome on our rank list and, in this scenario, itis more appropriate than a lower order outcome assignment.

15.6 Appendix D: Site Specific Protocol – Site 103 (Duke University Medical Center)

Protocol type: Site Specific Sub-Study

Parent Protocol: STeroids to REduce Systemic inflammation after infant heart Surgery (STRESS)

Site(s) engaged: Duke University (STRESS site 103)

Protocol Title: AKI protection with acetaminophen

Version/Date: Version 1.0/ 01 March 2019

Sub-study Background and Rationale:

Nearly 20,000 U.S. infants undergo congenital heart defect (CHD) surgery every year. Infant CHD surgery is associated with poor outcomes - mortality in ~3-5% and major morbidity in ~ 30%.[1] A major contributor to poor outcomes is post-operative acute kidney injury (AKI). Factors that contribute to post-surgical AKI include renal ischemia, reperfusion injury, oxidation, inflammation and cardiopulmonary bypass associated hemolysis.[2-5] Hemolysis from cardiopulmonary bypass is a major contributor that might be amenable to intervention. Hemolysis causes AKI by increasing plasma-free hemoglobin. This results in hemeprotein-mediated lipid peroxidation and renal vasoconstriction, thus producing renal injury.[2,6]

The risk of AKI may be reduced by perioperative administration of commonly used medications. For example, findings from in vitro and mouse studies demonstrate that acetaminophen reduces nephrotoxic hemoglobin radicals[7,8] and lipid peroxidation to decrease the incidence of AKI.[9] Further, in children undergoing cardiopulmonary bypass, acetaminophen attenuates markers of lipid peroxidation[6] and is associated with reduced odds of AKI.[10]

For many medications, including acetaminophen, the pharmacokinetics (PK) and pharmacodynamics (PD) are not defined in the post-operative CHD population for AKI prevention. For many commonly used medications, the PK and PD likely differ when used for prevention and/or treatment of AKI after CHD surgery as compared to healthy subjects. Therefore, a crucial step to ensure successful future studies is defining the PK and exposure-response profiles for the treatment/prevention of AKI in infants after CHD surgery.

The parent STRESS trial provides an ideal platform for the sub-study as the existing trial infrastructure and protocol can be leveraged without compromising the parent study operations or outcomes. All PK sampling can occur with the existing collection scheme and protocol without compromising the assay results. Furthermore, the existing parent trial protocol will capture nearly all data required to complete the sub-study. The modifications to the existing protocol do not incur any significant additional risks to the subjects. The primary modification is the addition of urine biomarker sample collection in the first 24 post-operative hours.

Study Design:

In subjects enrolled at Duke University who participate in the optional PK/PD and/or biomarker sampling, we will conduct a single-arm, open label standard of care dosing study of drugs affecting renal injury received in the first 24 hours after cardiopulmonary bypass -- primarily trageting acetaminophen, which is used commonly, but also to evaluate other potentially nephrotoxic or renal protective agents. Patient inclusion and exclusion criteria will be identical to the parent study. In addition to the already collected plasma samples, urinary biomarker samples will be collected and validated bioanalytical assays will be performed at a central lab.

Sampling Procedure:

Serum: No additional drug plasma samples will be collected during this study. As available, excess plasma from the parent study sampling scheme (see Table 5 of main protocol) will be used to characterize PK for medications (e.g. acetaminophen and metabolites) given per standard of care and associated with post-bypass renal protection.

Urine: Urinary biomarkers of renal injury, including NGAL, will be collected in sampling schemes noted in Appendix Table 1. Sampling will only occur for patients with indwelling urinary catheters at the time of sample collection.

Appendix Table 1: Urine biomarker sampling scheme

Sample Number	Time	Per patient urine collection
1	Pre-cardiopulmonary bypass (CPB)	1 x 3mL (minimum 1mL)
2	2-6 hours after completion of CPB	1 x 3mL (minimum 1mL)
3	18-24 hours after completion of CPB	1 x 3mL (minimum 1mL)

Sample Handling Procedures:

Similar to the parent study, assays to measure drug levels/metabolites in plasma, as well as biomarkers of renal injury in urine, will be conducted at a central lab using validate bioanalytical assays. For plasma, date and time will be recorded for the administration of parent study drug/placebo, acetaminophen and the acquisition time of the PK sample. For urine, date and time will be recorded for completion of CPB and acquisition time of the biomarker sample. All samples will be stored at -80°C until analysis.

Analytic approach:

Plasma PK data will be analyzed with a nonlinear mixed-effects model to determine drug and metabolite volume of distribution and clearance. Dose-exposure simulations will predict $AUC_{0\text{-}24}$. Linked PK/PD compartmental analysis will be performed to determine the acetaminophen exposure association to the primary pharmacodynamic outcome, staged KDIGO-defined AKI, and model optimal dosing. An exploratory pharmacodynamic outcome of concentration of urinary neutrophil gelatinase-associated lipocalin (NGAL) will also be included in analysis.

Safety Monitoring:

This amended sub-study involves the investigation of medications given as standard of care. An investigational new drug (IND) approval is not required. The investigators will monitor for adverse events through reports and laboratory values obtained per routine care.

References

1. Jacobs JP, Mayer JE, Jr., Pasquali SK, Hill KD, Overman DM, St Louis JD, Kumar SR, Backer CL, Fraser CD, Tweddell JS and Jacobs ML. The Society of Thoracic Surgeons Congenital Heart Surgery Database: 2018 Update on Outcomes and Quality. Ann Thorac Surg. 2018;105:680-689.
2. O'Neal JB, Shaw AD and Billings FTt. Acute kidney injury following cardiac surgery: current understanding and future directions. Crit Care. 2016;20:187.
3. Agarwal A, Dong Z, Harris R, Murray P, Parikh SM, Rosner MH, Kellum JA, Ronco C and Acute Dialysis Quality Initiative XWG. Cellular and Molecular Mechanisms of AKI. J Am Soc Nephrol. 2016;27:1288-99.
4. Cooper DS, Basu RK, Price JF, Goldstein SL and Krawczeski CD. The Kidney in Critical Cardiac Disease: Proceedings From the 10th International Conference of the Pediatric Cardiac Intensive Care Society. World J Pediatr Congenit Heart Surg. 2016;7:152-63.
5. Mamikonian LS, Mamo LB, Smith PB, Koo J, Lodge AJ and Turi JL. Cardiopulmonary bypass is associated with hemolysis and acute kidney injury in neonates, infants, and children*. Pediatr Crit Care Med. 2014;15:e111-9.
6. Simpson SA, Zaccagni H, Bichell DP, Christian KG, Mettler BA, Donahue BS, Roberts LJ, 2nd and Pretorius M. Acetaminophen attenuates lipid peroxidation in children undergoing cardiopulmonary bypass. Pediatr Crit Care Med. 2014;15:503-10.
7. Aronoff DM, Oates JA and Boutaud O. New insights into the mechanism of action of acetaminophen: Its clinical pharmacologic characteristics reflect its inhibition of the two prostaglandin H2 synthases. Clin Pharmacol Ther. 2006;79:9-19.
8. Gonzalez-Sanchez MI, Manjabacas MC, Garcia-Carmona F and Valero E. Mechanism of acetaminophen oxidation by the peroxidase-like activity of methemoglobin. Chem Res Toxicol. 2009;22:1841-50.
9. Boutaud O, Moore KP, Reeder BJ, Harry D, Howie AJ, Wang S, Carney CK, Masterson TS, Amin T, Wright DW, Wilson MT, Oates JA and Roberts LJ, 2nd. Acetaminophen inhibits hemoprotein-catalyzed lipid peroxidation and attenuates rhabdomyolysis-induced renal failure. Proc Natl Acad Sci U S A. 2010;107:2699-704.
10. Van Driest SL, Jooste EH, Shi Y, Choi L, Darghosian L, Hill KD, Smith AH, Kannankeril PJ, Roden DM and Ware LB. Association Between Early Postoperative Acetaminophen Exposure and Acute Kidney Injury in Pediatric Patients Undergoing Cardiac Surgery. JAMA Pediatr. 2018;172:655-663.