**Appendix 1. Executive Summary of Recommendations**

\* A functional whole blood test of anticoagulation, in the form of a clotting time, should be measured and should demonstrate adequate anticoagulation before initiation of, and at regular intervals during cardiopulmonary bypass. (Class I, Level of Evidence C)

\* Bolus administration of unfractionated heparin based upon weight is reasonable for achieving adequate anticoagulation, but individual response to heparin is heterogeneous and requires a therapeutic functional test of clot inhibition before initiation of CPB, independent of the bolus dose used. (Class IIa, Level of Evidence C)

\* It is reasonable to use Activated Clotting Time (ACT) tests that produce 'maximally activated' clotting times since these tests mitigate ACT variability, are less susceptible to hypothermia, and correlate more closely with Factor Xa activity compared to tests that employ a single activator. (Class IIa, Level of Evidence B)

\* It is reasonable to maintain activated clotting time above 480 seconds during CPB. However this minimum threshold value is an approximation and may vary based upon the bias of the instrument being used. For instruments using 'maximal activation' of whole blood or microcuvette technology, values above 400 seconds are frequently considered therapeutic. (Class IIa, Level of Evidence C)

\* Use of a heparin dose-response formula may identify reduced sensitivity to heparin, but has not been shown to be more useful than weight-based heparin dosing, in determining the heparin dose required to achieve an adequate ACT for initiation of CPB. (Class IIb, Level of Evidence B)

\* Use of heparin concentration monitoring in addition to ACT might be considered, for the maintenance of CPB, as this strategy has been associated with a significant reduction in thrombin generation, fibrinolysis, and neutrophil activation. However, its effects on postoperative bleeding and blood transfusion are inconsistent. (Class IIb, Level of Evidence B)

\* During CPB, routine administration of heparin at fixed intervals, with ACT monitoring, might be considered and offers a safe alternative to heparin concentration monitoring. (Class IIb, Level of Evidence C)

\* Clinical scoring estimates that use a fall in platelet count greater than 50% and/or a thrombotic event between 5 to 14 days following a heparin exposure can be used to determine whether a heparin-platelet antibody test should be performed to diagnose heparin-induced thrombocytopenia (Class IIa, Level of Evidence B)

\* Serum tests that include functional testing with serotonin release assay (SRA) or heparin-induced platelet activation (HIPA) can be beneficial in identifying patients with HIT who have a history of thrombocytopenia, and elevated clinical HIT risk scores, when PF4/heparin antibody testing is inconclusive (weakly positive) for HIT. (Class IIa, Level of Evidence C)

\* In patients who are seropositive for heparin-platelet antibodies or have a recent history of HIT, it is reasonable to delay elective cardiac operations requiring CPB until a patient's functional test and/or antigenic (antibody) assay are negative, with the expectation that heparin anticoagulation for CPB is likely to be safe and effective. (Class IIa, Level of Evidence C)

\* In patients with a diagnosis of HIT and in need of an urgent operation requiring CPB, anticoagulation with bivalirudin is a reasonable option. (Class IIa, Level of Evidence B)

\* In patients with significant renal dysfunction who are seropositive for HIT and require urgent operation requiring CPB, use of plasmapheresis, argatroban, or heparin with antiplatelet agents (such as tirofiban, ilioprost) may be considered, understanding that there are increased risks of bleeding with these interventions. (Class IIb, Level of Evidence C)

\* It can be beneficial to calculate the protamine reversal dose based upon a titration to existing heparin in the blood, since this technique has been associated with reduced bleeding and blood transfusion. (Class IIa, Level of Evidence B)

\* It is reasonable to limit the ratio of protamine/heparin to less than 2.6 mg protamine/100 Units of heparin, since total doses above this ratio inhibit platelet function, prolong ACT, and increase the risk of bleeding. (Class IIa, Level of Evidence C)

\* Because of the risk of heparin rebound in patients requiring high doses of heparin and with prolonged cardiopulmonary bypass times, low dose protamine infusion (25 mg/h) for up to 6 hours after the end of CPB may be considered as part of a multimodality blood conservation program. (Class IIb, Level of Evidence C)

\* In patients at high risk for anaphylactic response to protamine who experience pulmonary hypertension and circulatory collapse shortly after protamine administration, discontinuation of protamine and implementation of resuscitative measures including reinstitution of CPB with adequate anticoagulation may be lifesaving. (Class I, Level of Evidence C)

\* In patients requiring anticoagulation with bivalirudin who experience excessive bleeding after CPB, a combination of modified ultrafiltration, hemodialysis, and the administration of recombinant factor VIIa with blood product replacement may be considered to improve hemostasis in these extreme situations. (Class IIb, Level of Evidence C) (794 words)