Sepsis is a common and lethal disease – the 10th leading cause of death overall in the United States and septic shock being the leading cause of death in non-coronary intensive care units (ICU’s). Early and targeted fluid resuscitation in septic shock improves survival and mitigates the occurrence of acute respiratory failure. Colloid-based fluid resuscitation more rapidly achieves hemodynamic stability, improves oxygenation and may prevent edematous acute lung injury and acute respiratory distress syndrome (ALI/ARDS). Furthermore, from the sepsis subset of the 7,000 patients enrolled into the SAFE trial, albumin resuscitation was shown to improve survival with an odds ratio of 0.71 for all-cause mortality at 28 days (p=0.03) – an effect expected to be even greater for patients with septic shock. If proven to be of at least this magnitude, this improvement in survival translates to saving as many as 50,000 lives per year in the United States alone.

Determining the full clinical effectiveness of albumin resuscitation in patients with septic shock requires the conduct of a large, multi-centered, randomized, controlled clinical trial. In this proposal, we will complete a phase IIb clinical trial comparing albumin to normal saline for resuscitation in early septic shock, and in the process we will develop and pilot all the tools necessary to conduct a full effectiveness trial during the two year award period. Because septic shock is an acute and life-threatening condition that deteriorates rapidly and results in irreversible organ dysfunction or death, fluid resuscitation must be early and aggressive. The considerable experience of the two co-PI’s indicates that standard informed consent processes are unlikely to be adequate to successfully complete this trial, and thus we will incorporate necessary procedural steps to permit subject enrollment under an emergency exception from informed consent (EFIC). The complex and unique issues involved in resuscitation research and that will be addressed and planned in advance during this award include FDA regulatory and institutional review board approval to utilize EFIC; establishing the independent data monitoring committee and initiating the coordinating center; developing training materials, data documentation tools and investigational pharmacy procedures; establishing and piloting the organizational structures for clinical trial oversight; and finalizing the phase III study protocol with funding resources to complete the definitive phase III comparative effectiveness trial.