The FluidSync systems (pump + controller) will initially be made available commercially for biomedical and preclinical research and later for human use. This resubmitted proposal targets the technical feasibility of the animal pump and all reviewer comments were addressed.

2 BACKGROUND AND PHASE I TECHNICAL OBJECTIVES

2.1 Background

The FluidSync micropump consists of (a) an electrochemical actuator adjacent to and acting on (b) a bellows that separates the drug reservoir, whose outflow leads to (c) a catheter with a passive (mechanical), flow regulating check valve (Fig. 2). The reservoir is refillable by percutaneous injection through the refill port with a small diameter non-coring needle. The pump is wirelessly-operated by inductive power transfer. MEMS technology enables precisely machined parts with fine features in the nm-mm range for development of a miniaturized pump suitable for use in small animals[16, 17].

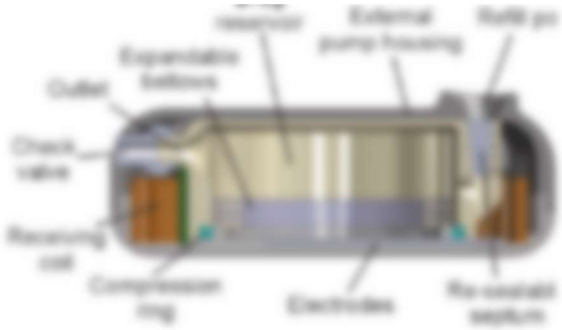

Figure 1. FluidSync micropump cross-section detailing the pump components.

The FluidSync LLC team has extensive experience in the development of implantable electrolysis-based micropumps for intraocular delivery of picoliter quantities of drug to rabbit eyes[18, 19] and rapid bolus delivery of cocaine in a self-administration paradigm rats[20, 21]. The team has also developed wireless telemetry for inductive power transfer to biomedical implants, including Class D and E systems. Using a wireless inductive power transfer system specifically developed for implantable microstimulators[22], we demonstrated real-time control of drug delivery *in vivo*[23]. A similar wireless system was effective for triggering a microvalve *in vivo* as part of a single-use subcutaneously-placed microbolus drug delivery pump used in mice[24-26]. Inductive power transfer (2 MHz) between an external primary coil and integrated secondary coil (either hand wound or on a printed circuit board (PCB)) was performed in both cases[23, 24]. A unique feature is that significant transfer of electrical power is possible over considerable distances between coils of very different sizes (20 cm and 1.6 cm diameters); this is made possible by phase-locking the oscillations of the primary inductive coil with the Class E oscillator. 150 mW could be generated on the secondary coil, far more than what is needed to trigger the valve which allowed triggering of the microvalve in the microbolus pump implanted in rats freely moving within a large cylindrical cage (33 cm in diameter). The team also demonstrated fabrication of secondary coils on printed circuit boards as well as microfabricated secondary coils embedded in Parylene C substrates and integrated with microelectronics[27, 28]. Previously developed systems will be modified and further miniaturized for use with FluidSync micropumps for mice.

2.2 Technical Objectives

The goal of the Phase I effort is to demonstrate both the technical and commercial feasibility of the complete FluidSync micropump system consisting of (1) the wirelessly operated and implantable electrolysis-based micropump, (2) external base station, and (3) software controller. At the conclusion, we will demonstrate the **first and only remote-controlled dosing technology** suitable for use in mice. The following technical requirements are motivated by customer input and organized around the most critical functional and operational features necessary for customer adoption.

Objective 1A: Miniaturization of pump components suitable for chronic implantation in mice.
Size and volume requirements: The pump must be < 10% of the animal's body weight to qualify as a minimally invasive implant. Standard adult laboratory mice typically weigh 30g. Experienced animal handlers highlighted the importance of minimizing the thickness of the implant which should be < 10 mm