Electronic Cigarettes: Are They Safe?, Principal Investigator Prudence Talbot. Ph.D. (20XT-0118) Abstract

Background: Electronic cigarettes (e-cigarettes) are nicotine delivery devices that have proliferated worldwide, untested for safety, at an alarming rate. They are readily available to adults, children, and teenagers via the Internet and in shopping malls. E-cigarettes consist of a battery that heats an atomizer that in turn aerosolizes nicotine and propylene glycol contained in a cartridge. Upon inhalation, the aerosol delivers nicotine into the user's lungs, after which residual aerosol is exhaled into the environment. E-cigarettes are often claimed to be safer than tobacco containing cigarettes because they deliver fewer chemicals to the user. However, this health claim has not been substantiated, and there has been no toxicological testing on the cartridge fluid and aerosol. Proposed work: Preliminary data show that heating cartridge fluid changes its chemical composition and that e-cigarette aerosol inhibits growth of human embryonic stem cells. These data combined with the absence of any biological toxicity data demonstrate the need for studies on the safety of e-cigarette cartridge fluid and aerosol. Using five brands of e-cigarettes, we will: (1) perform dose response experiments to determine what concentrations of cartridge fluid and aerosol are harmful to cultured cells using a novel bioassay that allows testing of multiple endpoints at one time, (2) identify and compare the chemicals in cartridge fluid and aerosol using analytical chemistry, (3) test the identified chemicals in the bioassay system to determine which are toxic, (4) quantify the concentrations of the chemicals in e-cigarette fluid and aerosol and correlate these with concentrations that are toxic in the bioassays. Bioassays will be done using cells from adult lung blood vessels, adult lung cells that line the airways, and, and human embryonic stem cells. Adult lung cells are chosen as they are one of the first cell types to contact inhaled aerosol and are therefore a prime target. Human embryonic stem cells are chosen as they model an early stage of human prenatal development which is one of the most sensitive stages in the life cycle to chemicals. Multiple dynamic cellular endpoints will be examined in dose response experiments using a novel state-of-the-art incubator (BioStation CT) that can capture video images of living cells during treatment. Data will be extracted from time lapse videos using specialized software tools. Significant differences in doses will be determined using well established statistical tests. Our bioassays will reveal the relative sensitivity of embryonic vs. adult cells to e-cigarette fluid and aerosol, the relative potency of fluid and aerosol for multiple cellular endpoints, what chemicals in e-cigarette fluid and aerosol affect these endpoints, if these effects can be reversed, and if toxic chemicals in ecigarette fluid and aerosol are present in high enough doses to bring about a harmful effect in a user based on the toxicological data. Benefits of outcomes: Our data will be the first to examine the toxicity of e-cigarette fluid and aerosol in cellular bioassays. This information is urgently needed as e-cigarettes are being sold worldwide with no understanding of product safety. Legislators attempting to regulate the use and distribution of e-cigarettes in our state, country, and other countries are doing so without information on the health benefits and health hazards that this product can produce. Our data will impact public policy and is urgently needed to help lead to rational regulation of e-cigarettes. Because e-cigarettes are also touted as a means to overcome nicotine addiction, our data may impact nicotine dependence treatments as well. Finally, our toxicity data will help clarify if the aerosol is safe to smoke and to release into the environment. It is essential to obtain objective data on e-cigarette safety as quickly as possible to

provide a basis for making responsible decisions regarding e-cigarette use world wide and to alert users to potential dangers.