Metals in Electronic Cigarette Aerosol
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Abstract:

Electronic cigarettes (EC) heat complex mixtures of flavor chemicals, and the effects of heating these mixtures on human health are not known. This supplemental project, which complements our existing R01, will identify and quantify reaction products formed from flavor chemicals during heating of EC fluids and determine which in vitro assays can best identify those flavor chemicals/reaction products that are harmful to the respiratory system. This objective will be conducted at two campuses with expertise in analytical chemistry (Portland State University-PSU) and human toxicology (University of California Riverside-UCR).
Aim #1 (PSU) will identify and quantify primary flavor chemicals and major flavor-derived pyrolysis/oxidation products formed during vaping of EC refill fluids and disposable EC. Fluids will be analyzed using gas chromatography/mass spectrometry (GC/MS), two-dimensional GC with MS (a method for complex component analysis), and liquid chromatography/MS/MS, which allows identification of low-volatility pyrolysis/oxidation products that cannot be determined by GC. Authentic standards will be used to identify/quantify all components present at □0.2 mg/mL. A variable-voltage tank EC will be used to “vape” refill fluids at several voltages. The resulting aerosol/vapor condensates will be analyzed to identify chemicals not found in the unvaped fluids and compared to chemicals on FDA’s *Harmful and Potentially Harmful Constituent List (HPHCL)*.
In Aim #2 (UCR), authentic standards of individual chemicals identified in Aim #1 in unheated EC fluids and aerosol condensates will be screened for cytotoxicity in dose response experiments using the MTT assay in conjunction with BEAS-2B lung epithelial cells isolated from normal human adults. Unheated EC fluids and their aerosol condensates will also be tested to verify that toxicity responses are similar in the isolated chemicals and the intact fluids/aerosol condensates. Lowest adverse effect levels, no adverse effect levels and IC50 values will be used to identify those flavor chemicals and the reaction products that are most cytotoxic.
In Aim # 3 (UCR), authentic standards of the most cytotoxic chemicals (Aim #2) will be tested using a multiplexing in vitro air-liquid interface (ALI) system that resembles a human lung. BEAS-2B cells or primary intact human bronchial epithelium will be exposed at an air-liquid interface to aerosols containing chemicals that are toxic in Aim #2. Dose response assays for the ALI system will examine: 1) survival, 2) stress protein synthesis, 3) inflammation, 4) ROS production, 5) ATP production, and 6) DNA damage. Data will establish the relative cytoxicity of each chemical in six mode-of-action assays and identify those assays that are best for detecting toxicity of flavor chemicals/reaction products using a lung model. In summary, this project will address both goals of FOA-PA-15-183 in that our data will identify and quantify flavor chemical degradation products produced during EC heating and determine which in vitro assays are capable of examining the harm potential of different flavorings that are heated in EC.