

Abstract:

This supplement is submitted in response to PA-15-183 which seeks to identify reaction products of flavor chemicals in electronic cigarette liquids (E-liquids) generated during heating and nebulization, and examine their potential toxicities. While many of the flavorings in E-liquids are generally recognized as safe in food, the safety of inhaled flavorings in E-cigarette users has not been established. Popular flavor mixes contain aldehydes such as cinnamaldehyde (cinnamon), carvone (spearmint) and terpenoids such as menthol (mint) and limonene (citrus). These chemicals are sensitive to oxidation and adduct formation which may occur when E-liquids are heated, vaporized or when stored for extended times. The nature and toxicity of flavor reaction products remains unknown. Aldehydes and other noxious chemicals are known to activate TRP ion channels, the chemical irritant receptors expressed in airway-innervating sensory nerves and in airway epithelia and vasculature. Reactivity and agonist activity towards TRP ion channels closely correlates with respiratory irritant activity and toxicity of chemicals, causing acute responses such as cough, pain and bronchoconstriction and promoting respiratory inflammation, or suppressing responses to irritants, thereby increasing exposures. Our preliminary data show that oxidized flavorings are more potent TRP activators and activate different receptors. Based on these findings, we propose to: Aim 1: Identify reaction products of E-liquid flavorings produced during heating and vaporization. Specific Aim 2: Compare responses of a TRP ion channel panel to E-liquids and their corresponding condensed vapors and, Aim 3: Examine the sensitivity of newly identified chemosensory receptors to flavorings and their products. The proposed studies will provide datasets to FDA supporting regulatory efforts aimed towards toxic constituents in electronic cigarettes.