

**Supplementary Table I Constituents Found in e-Cigarette Liquids and Aerosols and Their Physiological Effect on the Human Body**

<i>Constituent Properties</i>	<i>Effects on Body</i>
<p><i>Nicotine</i>: A colorless, odorless liquid water-soluble alkaloid with an oily consistency, acquires a brown color and gives off a strong odor of tobacco when exposed to air.</p>	<ul style="list-style-type: none"> <li>• Short-acting stimulant with rewarding and addictive properties.</li> <li>• Triggers the release of epinephrine from the adrenal glands and sympathetic response (increase in heart rate, blood pressure, etc.)</li> <li>• Lethal dose in children and adolescents remains unknown.</li> </ul>
<p><b>HUMECTANTS/SOLVENTS</b></p> <p><i>Propylene Glycol</i>: Clear, colorless, slightly syrupy liquid at room temperature. Practically odorless and tasteless, listed (GRAS) by the Food and Drug Administration (FDA).</p>	<ul style="list-style-type: none"> <li>• Allergic reactions, upper respiratory irritation, asthma.</li> <li>• Increased risk of toxicity in liver and kidney impairment and high-dose oral or intravenous administration.</li> <li>• No data for vapor inhalation &amp; absorption.</li> </ul>
<p><i>Glycerol (Glycerine)</i>: Oily, hygroscopic liquid with a warm, sweet taste.</p> <p>Less irritant than PG</p> <p>Listed GRAS by FDA</p>	<p>Mild headache, dizziness, nausea, vomiting, thirst and diarrhea at unspecified dosages</p>
<p><i>Ethylene Glycol</i>: An odorless, clear, slightly viscous liquid. Where present, it is at levels that are not likely to contribute significantly to adverse health effects.</p>	<ul style="list-style-type: none"> <li>• It is a respiratory irritant and is associated with markedly enhanced toxicological hazards when compared with conventionally used glycerol and PG</li> </ul>
<p><i>Flavorings</i>: More than 7,000 unique e-liquid flavors available. Concentrations vary widely. Fruity e-cigarette are often preferred among both smokers and non-smokers. Diacetyl, acetylpropionyl (2,3-pentanedione), acetoin, Cinnamaldehyde are chemicals used. Often named as a primary reason for e-cigarette use.</p>	<ul style="list-style-type: none"> <li>• Flavors may have cooling and local anesthetic effects</li> <li>• Reasons for uses include increased satisfaction and enjoyment, variety and customization, better feel and taste than cigarettes, food craving suppression, social impacts.</li> <li>• Menthol reinforces effects of nicotine on tobacco smoking behaviors - results in increased nicotine dependence and a greater chance of tobacco-attributable disease.</li> <li>• Formation of aldehydes—vanillin and ethyl vanillin, thujone, menthol (pulegone, eucalyptol) which is associated with adverse respiratory health outcomes. Increased incidences of chronic cough, bronchitis, asthma, and bronchiolitis obliterans.</li> <li>• Even at low concentrations, cinnamaldehyde in e-cigarette products is cytotoxic, genotoxic, adversely affects cell</li> </ul>

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	processes and survival. It may also impair homeostasis in the respiratory system.
<i>Carbonyl compounds:</i> Formaldehyde, Acetaldehyde, Acrolein, Glyoxal, Propanal, Crotonaldehyde, Butanal and Methylglyoxal which have been found in e-cigarette aerosols. Aerosols generated from PG-based e-liquids were found to have the highest levels of carbonyls. Compared to combustible cigarettes, very high levels of formaldehyde are found in aerosols from E-cig	<ul style="list-style-type: none"> <li>• Lower liquid levels within the cartridges or tanks may increase air flow and promote overheating of the wire if no safety features are incorporated to maintain a constant and lower temperature. This leads to the formation of carbonyls, which are potentially hazardous and/or carcinogenic</li> </ul>
<p><i>Minor Tobacco Alkaloids:</i> Impurities including minor alkaloids: Nornicotine, Anatabine, Anabasine, Cotinine, Nicotine <i>N</i>-Oxides, Myosmine, Nicotyrine and Nornicotyrine.</p> <p>These minor alkaloids may arise from biosynthetic processes in the living tobacco plant or by bacterial action or oxidation during tobacco processing and can thus be found in e-cigarette liquids derived from tobacco products</p>	Nicotine-related impurities are thought to be less toxic than nicotine
<i>Tobacco-specific nitrosamines:</i> <i>N</i> '-nitrosoanatabine (NNN), NNK, <i>N</i> '-nitrosoanabasine (NAB). TSNAs are potent carcinogenic chemicals.	Carcinogenic potential
<i>Free Radicals and Reactive Oxygen Species (Ros):</i> Activating the e-cigarette's heating element and aerosolizing the e-liquid produces ROS; these species are drawn into the lungs directly from the device. Oxidants are also derived from a device's lithiumion battery, similar to that used in combustible tobacco cigarette filters and e-cigarette cartomizers	They cause oxidative stress, which damages cellular proliferation, metabolism, and health, and can be involved in the development of several cardiovascular, respiratory neurodegenerative disorders, rheumatoid arthritis, and some types of cancers.
<i>Volatile Organic Compounds (Vocs) And Phenols:</i> Benzene, Toluene, Ethylbenzene, <i>M</i> -Xylene, <i>P</i> -Xylene, <i>O</i> -Xylene, Styrene, Ethyl Acetate, Ethanol, Methanol, Pyridine, Acetylpyrazine, 2,3,5-Trimethylpyrazine and  Octa- Methylcyclotetrasiloxane	<ul style="list-style-type: none"> <li>• Irritant to upper and lower respiratory tract</li> <li>• Central nervous system and end-organ damage at high concentrations</li> <li>• Carcinogenic potential</li> </ul>
<i>Residual Solvents:</i> The thermal degradation of sugars can produce toxic furans, such as 5-hydroxymethylfurfural and furfural	<ul style="list-style-type: none"> <li>• Irritant to Upper Respiratory Tract</li> </ul>
<i>Polycyclic aromatic hydrocarbons (PAHs):</i> Products of combustion which can form small particles or bind to other small particles	<ul style="list-style-type: none"> <li>• Irritant to Upper Respiratory Tract</li> <li>• Carcinogenic potential</li> </ul>

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<p><i>Phthalates:</i> Diethyl phthalate (DEP) and diethylhexyl phthalate (DEHP)</p> <p>IARC classifies DEHP as “possibly carcinogenic to humans”.</p>	<ul style="list-style-type: none"> <li>• These antiandrogenic, estrogen-like compounds have been shown to lead to gynecomastia</li> </ul>
<p><i>Metals:</i> Chromium, Nickel, Lead, Manganese, Aluminum, Tin, and Iron in e-liquid emissions originate from several parts of the device, including the metallic coil, a complex alloy that heats the e-liquid to produce the aerosol that is inhaled by the user. Lead, Nickel, Tin quantified at significantly higher concentrations in e-cigarette aerosols than combustible tobacco smoke</p>	<ul style="list-style-type: none"> <li>• Specific Metal related toxicities</li> </ul>
<p><i>Caffeine:</i> E-liquid flavors like coffee, tea, chocolate, and energy drinks.</p>	<ul style="list-style-type: none"> <li>• Very little is known about the effects of caffeine inhalation, and health risks cannot be estimated.</li> </ul>
<p><i>Pharmaceutical drugs:</i> Weight loss medication (Rimonabant) not approved by FDA (2007) has been found in e-liquids. E-liquids can contain an analogue (amino tadalafil) active ingredient found in Cialis, an erectile dysfunction drug</p>	<ul style="list-style-type: none"> <li>• Adverse neurological events such as seizures and suicide</li> <li>• Undetermined or harmful health effects</li> </ul>
<p><i>Microorganisms:</i> Bacteria, fungi, parasites</p>	<ul style="list-style-type: none"> <li>• Presence of micro-organisms could lead to bacterial/fungal/parasitic infections</li> </ul>

*Adapted from: Eaton DL, Kwan LY, Stratton K, editors. Public Health Consequences of E-Cigarettes-Toxicology of E-Cigarette Constituents. National Academies Press (US). 2018; 5*