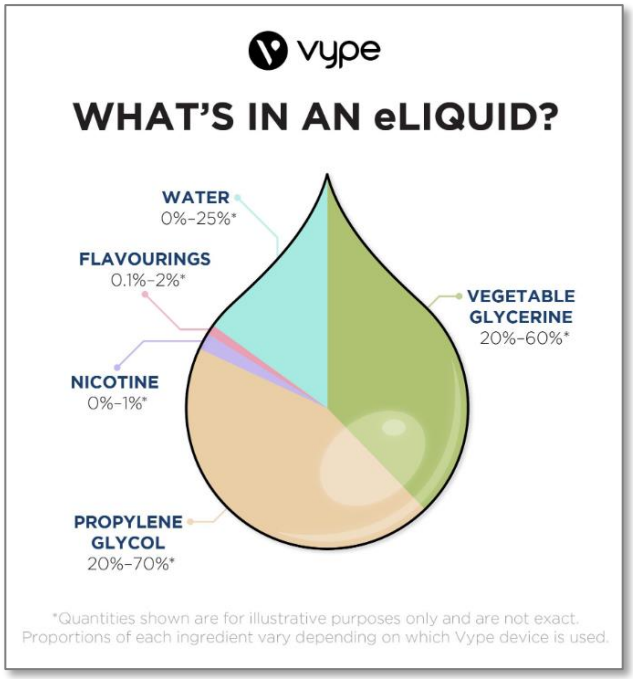
Propylene glycol & vegetable glycerin

Old and new evidence that these chemicals are not safe to inhale

Propylene glycol (PG) and vegetable glycerin (VG), also known as glycerol, are chemical compounds present in nearly all e-cigarettes and vaping products. Recent reports of acute respiratory disease among some users of vaping products have raised questions about whether these chemicals are safe to inhale.



PG and VG are common chemicals that have been in everyday use for many decades. They have applications in food processing, as food additives and as additives in cosmetics and pharmaceuticals. They are also used in antifreeze and have other industrial applications. For all food applications they are designated by the US Food and Drug Administration as "generally recognized as safe" (GRAS) for ingestion, but not necessarily for other forms of exposure, like inhalation.[1]

Prior to the development of e-cigarettes, propylene glycol and vegetable glycerin were never used in aerosols intended for repeated inhalation. PubChem list dozens of approved uses of glycerol in consumer and industrial products. None of them involve inhalation of the substance.[2] E-cigarette manufacturers were not required to conduct inhalation toxicity testing of these aerosols, and none of them are known to have done so.

Early cautions about inhaling propylene glycol and vegetable glycerin

Since glycerol was never intended to be inhaled in a hot aerosol, there is little inhalation toxicology of the substance that predates the appearance of e-cigarettes. Because some of the uses of propylene glycol that involve inhalation do predate e-cigarettes, there is some inhalation toxicological information available for that compound.

No health authority has labelled propylene glycol safe for inhalation. Manufacturers and chemical safety agencies recommend that inhalation be avoided, as shown in the Table 1.

Despite these cautions against inhalation of propylene glycol, its use is common in theatrical fog machines. However, in persons regularly exposed to theatrical fog, glycol-containing fog machines have been observed to produce acute cough, dry throat, increased acute upper airway symptoms and decreased lung function.[3]

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Propylene glycol in cigarettes

Although propylene glycol has long been used as an additive in cigarettes, and has been found to produce cancer-causing chemicals when burned, [8] this experience has very little bearing on its potential hazards in e-cigarettes. The chemicals produced by burning will likely be different than the chemicals produced from heating without burning. Moreover, almost all of the propylene glycol used in cigarettes never finds its way into cigarettes, as combustion transforms it into other compounds.[9]

Table1: Selected information about the inhalation of propylene glycol from one commercial and three government agencies

Agency	Selected quotation on effects of inhalation of propylene glycol
Dow Chemical[4]	"Mist may cause irritation of upper respiratory tract (nose and throat)."
European Chemicals Agency[5]	"Avoid inhalation of hot vapours or extremely high concentrations of aerosols."
Institut national de recherche scientifique (INRS) France[6]	"Le propylène-glycol présente peu de risques dans les conditions normales d'utilisation. Toutefois, des mesures de prévention sont nécessaires dans certaines situations, en particulier si le produit est utilisé à chaud, s'il peut y avoir formation d'aérosols" "En cas d'inhalation de fortes concentrations, retirer le sujet de la zone polluée. Prévenir un médecin en cas de trouble."
ILO/WHO/EU International Programme on Chemical Safety[7]	"Avoid inhalation of mist and vapour. Use ventilation."

Recent concerns about propylene glycol and vegetable glycerin in e-cigarettes

The US Centres for Disease Control provided information on 573 cases of vaping-related illnesses in the USA and concluded that "the specific chemical exposure(s) causing lung injuries associated with e-cigarette product use, or vaping, remains unknown at this time." [10]

Reports of acute illnesses and deaths have increased interest in the health risks of inhaling propylene glycol and vegetable glycerin.

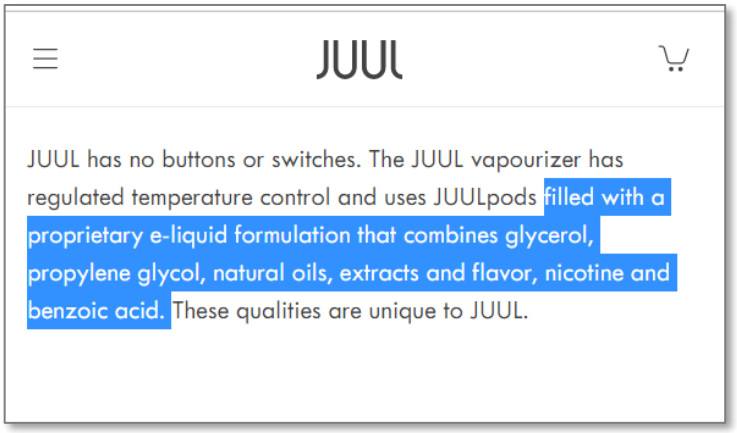
In early August 2019, the United States Food and Drug Administration (USFDA) invited comments on a proposal to add 19 chemicals to the official list of Hazardous and Potentially Hazardous Chemicals (HPHC) in tobacco products (including e-cigarettes).[11] Among the 19 chemicals which the FDA proposes to identify as potentially hazardous are propylene glycol and glycerol.

In support of identifying these chemicals as potentially hazardous, scientists at the University of California in San Francisco cited recent and older studies which had linked these compounds to health harms.[12]

PG and VG can introduce harmful fat to the lungs.

- A 2012 American study reported a case of lipoid pneumonia (fat particles in the lung) which resulted from glycerin-based oils in e-cigarettes.[13] Reports on several other U.S. cases were published in 2019,[14] [15] as were earlier cases in the United Kingdom.[16]

- A 2019 study exposed mice to e-cigarettes made with no flavours, with and without nicotine, but with propylene glycol and vegetable glycerin (PG/VG). Irrespective of the presence of nicotine, fat globules built up in the lungs of the mice.[17] Moreover, the immune systems of the mice lungs were impaired, leaving them vulnerable to infections. This triple effect of PG/VG (fat globules and impairment of lung immune systems, and subsequent vulnerability to further infection) suggests there may be complex and multiple pathways leading from exposure to disease. This possibility is acknowledged by the US CDC which recently stated that the current outbreak of vaping-related disease and death "might have more than one cause."[10] It should also be noted that propylene glycol and vegetable glycerin are not "contaminants." They are main ingredients in e-cigarette liquids.



PG and VG can irritate and harm lung tissue

- A 2001 Swedish study found that short-term exposure to propylene glycol irritates the airways.[18]
- Australian medical researchers recently examined some of the health effects of vaping.[19] They examined the effects of 11 different chemicals or combinations of chemicals on human bronchial cells. All, including propylene glycol and glycerol, caused adverse effects on the bronchial cells.
- Respirologists based in California recently published a comprehensive review of the respiratory effects of e-cigarettes.[20] They concluded that recent research demonstrates that propylene glycol and vegetable glycerin damage airway epithelia and cause other adverse effects on the respiratory system and that "saying with certainty that e-cigarettes are safer than combustible cigarettes is impossible."

When heated, PG and VG can create toxic chemicals

- A 2017 study by researchers at the California Department of Public Health showing that propylene glycol and glycerol in e-cigarettes led to the creation of toxic chemicals, like formaldehyde and acetaldehyde.[21]
- In its review of the Public Health Consequences of E-Cigarettes, the National Academies of Sciences Engineering and Medicine concluded that when propylene glycol, glycerine and other chemicals in "e-liquids are heated and aerosolized, they can produce chemical reactions that could form carbonyl compounds such as reactive aldehydes, which are considered to have toxic effects on human health."[22]

A knowledge void

The U.S. Food and Drug Administration requested the National Academies of Sciences Engineering and Medicine (NASEM) to review e-cigarettes. Their 2018 report noted the absence of studies on the long-term health effects of propylene glycol. *"No epidemiological studies have addressed the long-term health consequences, including cancer, of propylene glycol and glycerol. Despite the fact that propylene glycol has been widely used in theatrical settings and in a few other occupations, … the*

absence of evidence on cancer related to this topic is demonstrated by the fact that the Department of Health and Human Services, the International Agency for Research on Cancer, and the Environmental Protection Agency have yet to classify the carcinogenicity of propylene glycol in humans."

Many of the hazard reviews that have taken place have focussed especially on cancer risks. However, this emphasis may be misplaced when considering the hazards of propylene glycol and glycerin in the form of a repeatedly inhaled heated aerosol. A recent review of the non-cancer related respiratory effects of e-cigarettes highlighted this problem. "*The effects of e-cigarettes have similarities to and important differences from those of cigarettes. Decades of chronic smoking are needed for development of lung diseases such as lung cancer or chronic obstructive pulmonary disease, so the population effects of e-cigarette use may not be apparent until the middle of this century. We conclude that current knowledge of these effects is insufficient to determine whether the respiratory health effects of e-cigarette are less than those of combustible tobacco products*."[19]

Vaping products are differently harmful than cigarettes

Even though inhalation of propylene glycol aerosol has long been known to be hazardous, caution statements were ignored by manufacturers and governments alike when these products were used in e-cigarettes. Prior to the appearance of e-cigarettes in the marketplace, vegetable glycerin was never used or contemplated for use in any application that involved inhaling it as a component of a heated aerosol. The limited toxicological information now available on vegetable glycerin points to toxic effects on the respiratory system.

Propylene glycol and vegetable glycerin in aerosols may yet be shown not to be involved in the causation of the current wave of vaping-related acute pulmonary illnesses in the USA and Canada. Even if they are not responsible for these acute lung illnesses, they cause changes to the respiratory system that could lead to chronic lung diseases over a longer period of time.

Vaping products contain propylene glycol, vegetable glycerin and other products not usually found in cigarette smoke. As a result, we cannot draw on research on the effects of tobacco smoking to make conclusions about the harms or safety of inhaling these compounds.

Heating up a mixture of substances known to be poisonous when inhaled, including propylene glycol and vegetable glycerin, and then inhaling the mixture as an aerosol, is not a safe behaviour. It was never a safe behaviour. Vaping products that use these compounds should not be spoken of as being "less harmful" than combusted tobacco, they should be considered "differently harmful."

Key points to remember

- Propylene glycol (PG) and vegetable glycerin (VG, glycerol) are the main components of e-cigarettes liquid. They are hazardous when inhaled and this has been known for a long time.
    - Burning propylene glycol in cigarettes produces carcinogens.
    - Heating PG and VG in e-cigarettes produces lung disease hazards not previously observed in cigarette smokers.
- Recent evidence suggests that inhaling these compounds makes lungs vulnerable to infections from contaminants from other sources.

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