Electronic cigarettes or e-cigarettes are battery operated nicotine delivery devices that are designed and used in a similar fashion as conventional cigarettes. These devices are presumed to deliver nicotine rapidly to its users without exposure to the many harmful chemicals present in conventional cigarettes.

A shisha pen (electronic hookah, e-hookah or hookah pen) is an electronic vapourizer just like an e-cigarette. The products are indistinguishable from e-cigarettes, given that they are available with and without nicotine and the system of operation is almost the same.

What are the components of e-cigarettes?

E-cigarettes are composed of three parts (Figure 1):

1) A cartridge is used to store liquid material and contains the flavored nicotine called the “e-liquid”, “e-juice” or “nicotine solution”. The cartridge serves as a reservoir of storage for the nicotine liquid and also acts as the mouthpiece of the e-cigarette. Two types of e-liquids are available: synthetic, containing artificial flavours and solvents and natural, containing extracts of tobacco leaves and natural flavours extracted from plants (Etter, 2013).

2) An atomizer is used as a heating element and it turns the liquid into a vapour form.

3) A power source such as a battery or a wired USB device. The power source can be either manual or automatic. Manual e-cigarettes require activation of the heating element by pushing a button, while automatic batteries are activated by sucking in air.

Figure 1: Components of an e-cigarette
How do e-cigarettes work?
E-cigarettes use a heating element to vapourize nicotine and other ingredients, simulating the visual, sensory, and behavioural aspects of smoking without the combustion of tobacco. The user inhales the mist or vapour generated by drawing on the mouthpiece and activating the heating element which vapourizes the liquid. The vapour is only produced while the heating element is activated and not between puffs (DKFZ, 2013).

What temperatures are needed to generate the 'vapour'?
The vapour is generated by heating element to temperatures ranging from 65°C to 120°C (DKFZ, 2013), with reported maximum atomizer temperature of approximately 250°C (MEC, 2013).

Are all e-cigarettes the same?
No, there are hundreds of different brands of e-cigarettes in the market; both disposable and rechargeable. These vary in size, shape, color and cartridge system design. These systems include pre-filled replacement cartridges, open cartridges, or dropper bottles with refill liquid (DKFZ, 2013). Significant variability has also been reported between and within brands in the airflow rate required to produce aerosol, pressure drop, length of time cartridges lasted, and production of aerosol. Variation in performance properties within brands suggests a need for better quality control during e-cigarette manufacture (Williams and Talbot, 2011).

Do e-cigarettes come in different flavours?
Yes, disposable e-cigarettes and e-liquids come in a variety of flavours included but not limited to cherry, apple, grape, strawberry, banana, mango, coffee, almond, coconut, chocolate, vanilla, mint, jasmine, piña colada, bubble gum, cinnamon, cola and many more (Figure 2).

How many puffs can you get from an e-cigarette, in comparison to a conventional cigarette?
A regular cigarette can be smoked in approximately 13 puffs (Djordjevic et al., 2000). The number of puffs in an e-cigarette is dependent on personal smoking habit and use, but generally an e-cigarette user gets less than 60 puffs per mL (ECF, 2013). Rechargeable e-cigarettes can provide from 800 to 1000 puffs (ES, 2013), while disposable e-cigarettes can provide between 300 to 500 puffs (ESS, 2013).

Is smoking e-cigarettes different than conventional cigarettes?
Yes, e-cigarettes require sucking harder than conventional cigarettes, particularly when the amount of liquid in the cartridge is low resulting in a puff duration of 4.3 seconds, in comparison to 2.4 seconds as with tobacco cigarettes (Hua et al., 2013).

How much do e-cigarettes cost?
E-cigarettes vary greatly in price from as low as €4.76 (EBN, 2013) to over €100 (ESS, 2013). A disposable cigarette of €5.95 with 300 puffs (ESS, 2013) results in €0.02 per puff, in comparison to a conventional cigarette of around €5.50 for 19 cigarettes with around 13 puffs/cigarette (Djordjevic et al., 2000) resulting in €0.02 per puff.

Where can you buy e-cigarettes?
E-cigarettes can be purchased anywhere from small kiosks and stores to online.

Figure 2. Example of a few e-cigarette flavours
How are e-cigarettes regulated?

E-cigarettes are regulated as a recreational product under the 'Warenwet', and are not strictly regulated as with tobacco products and medicines.

Users and perceptions

How many people use e-cigarettes in The Netherlands?

Statistics show that in The Netherlands 1% of people use e-cigarettes occasionally, 5% tried it once or twice and 94% have never tried it (EC, 2012, STIVORO, 2012).

What is the current awareness of e-cigarettes in The Netherlands?

In The Netherlands, 55% of people have heard of e-cigarettes and know what they are (EC, 2012).

What is the attitude of Europeans in regards to the harmful health effects to those who use them?

In Europe, 38% of European citizens don’t know whether e-cigarettes are harmful, 35% think they are not harmful, while 27% think they are harmful to the health of those who use them (EC, 2012).

Is there concern that e-cigarettes might be a gateway for young people to smoke conventional cigarettes?

Health experts around the world have expressed concern that e-cigarettes are marketed towards young people given that some of the devices look nothing like conventional cigarettes and come in attractive colors such pink, purple, white, black, red, and blue with flavours such as chocolate, strawberry and bubble gum. Some e-cigarettes have fancy buttons or lamps in a shape of a diamond simulating an attractive gadget and not a cigarette. Some designs look more like fancy coloring pens than e-cigarettes (Figure 3). In addition, the majority of products do not have health warning labels to better inform people. E-cigarettes are rarely regulated and do not fall under the conditions of tobacco laws and because of this, they can be sold anywhere from small kiosks and stores to online.

Is there an age limit for buying e-cigarettes?

Although e-cigarettes are intended for people over the age of 18, there is no real control to verify this. Currently, there is no law to enforce the age limit.

Is there a ‘for adult use only’ warning in the wrapper or cartridge label?

Many online providers have warnings such as ‘not intended for people under the age of 18’ and studies have shown that approximately 55% of cartridges (11 out of 20 cartridges analyzed) had a ‘for adult use only’ warning in the label (Cheah et al., 2012).

Is there any information on the age-distribution of e-cigarette users?

A study in the UK showed that 1% of e-cigarette users were between the age of 18 to 30, 55% were between the age of 31 and 50, and 32% were over the age of 50 (ECD, 2013)
Addictive properties and use as cessation product

Are e-cigarettes addictive?
Yes, similar to nicotine in conventional cigarettes, nicotine in e-cigarettes is addictive. Nicotine is a major component of e-cigarettes and it binds to nicotine receptors in the brain to release neurotransmitters that stimulate the reward centre, resulting in a feeling of well-being and pleasure. With continuous use, this can result in nicotine cravings and dependence. Because nicotine dependence has a physical and psychological component, it is challenging to quit (DKFZ, 2013).

What is nicotine? And why is it commonly used as an aid to stop smoking?
Nicotine is responsible for the addictive properties of tobacco smoking. Inhaled nicotine is absorbed through the pulmonary rather than the systemic venous system resulting in nicotine reaching the brain in 10 to 20 seconds (Benowitz, 1996). Nicotine binds to nicotinic cholinergic receptors in the brain which in turn release a variety of neurotransmitters which stimulate the reward centre and brings about a feeling of a pleasurable experience, induced stimulation and pleasure, reduced stress and anxiety, arousal, mood control, and improvement in concentration, reaction time and performance in certain tasks (Benowitz, 1996). People smoke to deliver desired doses of nicotine to their bodies and when a person stops smoking, nicotine withdrawal symptoms emerge including irritability, depressed mood, restlessness, anxiety, problems getting along with friends and family, difficulty concentrating, increased hunger and eating, insomnia, and tobacco cravings (Benowitz, 1996). For this reason, nicotine replacement therapies (NRTs) (gum, transdermal patch, nasal spray, inhaler, sublingual tablet and lozenge) are often used as aids to quit smoking. Most NRTs relieve nicotine withdrawal symptoms but most deliver nicotine to the brain at a slower rate than with tobacco smoke.

Are there warnings present on nicotine addiction in the wrapper or cartridge label?
Generally, there are no warnings with regards to nicotine addiction in the wrapper or cartridge labels (Cheah et al., 2012). 

Are e-cigarettes a possible nicotine replacement therapy?
Surveys indicate that e-cigarettes can reduce cravings and withdrawal symptoms, even e-cigarettes without nicotine reduce the desire to smoke and withdrawal symptoms and some smokers cut down smoking or quit smoking as a result of using e-cigarettes. Nevertheless, the efficacy of e-cigarettes as an aid for sustained smoking cessation has not yet been proven. More research is needed on the efficacy of e-cigarettes as a cessation device (DKFZ, 2013, Etter, 2013).

What are the most common aids used to stop smoking in The Netherlands?
European statistics show that in The Netherlands, 73% of smokers try to quit without assistance, 22% of smokers use nicotine replacement medications such as nicotine patches, nicotine gum, nicotine inhaler or other medications and 7% of smokers use e-cigarettes or smokeless cigarettes (EC, 2012).

Is there evidence that nicotine is delivered consistently throughout the various e-cigarette puffs?
In a recent study, the nicotine levels of vapours generated by mimicking the smoking conditions of real e-cigarette smokers were evaluated from 16 of the most popular e-cigarettes in Poland, UK, and US markets. Results showed that the total level of nicotine in the vapour was generally effectively delivered during the first 150 to 180 puffs, with an average of 50 to 60% of nicotine being vapourized (Goniewicz et al., 2013). E-cigarette brands and models varied significantly in their efficacy and consistency of nicotine vapourization where some brands vapourized nicotine effectively up to 70% while others were very inefficient vapourizing nicotine to only about 30% (Goniewicz et al., 2013). In addition, the dose of nicotine delivered with each puff varied substantially (FDA, 2009). Three different e-cigarette cartridges with the same label were tested and each cartridge emitted a markedly different amount of nicotine with each puff ranging from 26.8 to 43.2 mcg nicotine/100 mL puff (FDA, 2009).

How much nicotine is in e-cigarettes?
E-cigarettes (disposable or rechargeable) contain reported nicotine levels varying from 0 to 36 mg/ml (DKFZ, 2013). The nicotine strength of the e-liquid can vary with every brand but generally there is a low (6 mg), medium (11-12 mg), high (16-18 mg), extra high (24 mg) and super high (36 mg). The e-liquid can also be sold in different volumes ranging from 10 to 100 mL. Nicotine can be lethal to adults with an acute intake of 30 to 60 mg, while an acute intake of 10 mg of nicotine is lethal for children.

Are the levels of nicotine in the label consistent to the measured nicotine levels?
The majority of studies have shown poor consistency between actual measured nicotine levels in e-cigarettes cartridges and
e-liquids and the amount of nicotine in the label (Cheah et al., 2012, Trehy et al., 2011, Goniewicz et al., 2013). Others report consistency between nicotine content in the e-cigarettes and e-liquid, and the labels on the bottles (Etter et al., 2013). Of concern is the presence of nicotine in e-cigarette cartridges or e-liquids reported to be nicotine free (Cheah et al., 2012, FDA, 2009). Analysis by the US FDA also found the one high nicotine cartridge delivered double the nicotine dose (FDA, 2009). These inconsistencies may pose harm to e-cigarette users.

**Health and safety information**

**Is there any disposal information of the product?**

Currently, there are no methods for proper disposal of e-cigarette products and accessories, including cartridges, which could result in nicotine contamination from discarded cartridges entering water sources and soil, and adversely impacting the environment.

**What is in the e-liquid? And are any of the components toxic?**

Contents of the e-liquid are made up of water, nicotine and flavorings in propylene glycol or glycerin. Here we review the toxicity information of nicotine, propylene glycol, glycerol and impurities present in the e-liquid.

**Nicotine:** Nicotine can be lethal to adults with an acute intake of 30 to 60 mg, while an acute intake of 10 mg of nicotine is lethal for children. Depending on nicotine content, nicotine intoxication can occur if liquid enters the mouth when smokers inhale too hard in the device or dermal exposure when replacing cartridges. Recently, a toddler died after ingesting an e-liquid in Jerusalem (Eisenbud, 2013). Nicotine intoxication is also possible by taking too many puffs (DKFZ, 2013). Nicotine is not considered a direct cancer-causing chemical but evidence suggests that nicotine may be a tumor promoter by inhibiting cell death and promoting new blood cell formation in animal studies (Benowitz, 2009).

**Propylene glycol:** Propylene glycol is a major ingredient in e-cigarettes. Volunteers exposed to propylene glycol mist for 1 minute showed upper airway irritation (Wieslander et al., 2001). Propylene glycol levels in e-cigarettes range from 0-1320 mg/cartridge (Cheah et al., 2012). E-cigarettes which had zero levels of propylene glycol had 444 mg/cartridge of glycerol (Cheah et al., 2012). It is not clear if irreversible effects will occur in humans given the high concentration of propylene glycol per cartridge. Studies in rats exposed to concentrations similar to those found in e-cigarettes showed irreversible respiratory damage (Suber et al., 1989). Limits for propylene glycol by actors exposed via theatrical fog has been set at 40 mg/m³ (ToxNet, 2013), and this limit is often exceeded when smoking e-cigarettes. Diethylene glycol is found as an impurity left from the manufacturing process of propylene glycol and vegetable glycerin and is poisonous to humans. Diethylene glycol was detected in one out of forty seven (2%) cartridges in an inventory performed by the US Food and Drug Administration (FDA) (FDA, 2009).

**Glycerol:** Glycerol levels in e-cigarettes range from 19.4 to 1020 mg/cartridge (Cheah et al., 2012). There were no human inhalation studies with glycerol found. Animal studies of rats exposed to glycerol report irritation to the upper respiratory tract at concentrations present in e-cigarettes (Renne, 1992). Glycerol also induced squamous metaplasia of the epiglottis in rats following repeated exposure to concentrations present in e-cigarettes (Renne, 1992). Squamous metaplasia is a reversible change from one cell type to another cell type as a response to chronic stress as often seen in the airways of smokers. Metaplasia is generally a reversible process where cells return to normal after the stress has been removed but in a few cases cancerous (malignant) degeneration of the newly formed tissue may result.

**Impurities:** Several impurities such as tobacco-specific impurities (anatabine, anabasine, nornicotine, beta-nicotyline, nicotine, N-oxide, cotinine, and myosmine) and trace levels of carcinogenic tobacco-specific nitrosamines such as 4-(methyl nitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N′-nitrosornicotine (NNN) have been found in e-cigarettes (Etter, 2013, DKFZ, 2013). In a 10 minute smoking session, carbonyls such as acetaldehyde, formaldehyde, acrolein, propanal, butanal, glyoxal and methylglyoxal have been detected in e-cigarettes (Uchiyama et al., 2010). High concentrations of short-chain aldehydes such as formaldehyde, acetaldehyde and acrolein are produced during the heating of e-cigarettes (Cheah et al., 2012).

NNK, NNN and Formaldehyde are known human carcinogen (Group 1) classified by the International Agency for Research on Cancer (IARC) (IARC, 2006), while acetaldehyde is classified as a possibly carcinogenic to humans (Group 2B) (IARC, 1997)

**Are there any side-effects to smoking e-cigarettes?**

Side effects of e-cigarettes include mouth and throat irritation, dry cough, dizziness and nausea; all of which generally subside over time (DKFZ, 2013). The US FDA has received 47 reports from which 8 (17%) were severe adverse effects such as pneumonia, congestive heart failure, burns due to explosion of the product, possible infant death secondary to choking on an e-cigarette cartridge (Chen, 2013). In addition, in September 2010, the US FDA issued a number of warning letters to e-cigarette distributors for various violations of the Federal Food, Drug and Cosmetic Act including violations of good manufacturing practices, making unsubstantiated drug claims, and using the devices as delivery mechanisms for active pharmaceutical ingredients (FDA, 2010).
Are the published health benefits true?
No, not all the advertised claims are true. Here are a few examples of misleading information.

Health benefits same as when you quit smoking
This is not known as there are many cancer causing chemicals still present in e-cigarettes.

No more cough and phlegm
False: Mouth and throat irritation, dry cough, dizziness and nausea are the most common side-effects of e-cigarette use; all of which generally subside over time (DKFZ, 2013). In addition, propylene glycol and glycerol are the main ingredients in the e-liquid and both compounds are strong irritants and are present in high concentrations in e-liquids (Cheah et al., 2012). The main effect of propylene glycol exposure in levels present in e-cigarettes is cough and upper airway irritation (Wieslander et al., 2001).

No tobacco (Geen tabak)
False: Some natural e-liquids contain extracts of tobacco leaves (Etter, 2013).

No Cancer (Geen kanker)
This is not known given that there are several tobacco-specific nitrosamines such as NNK and NNN present in e-cigarettes which are known human carcinogens. In addition, formaldehyde (a known human carcinogen) and acetaldehyde (a possible human carcinogen) are also present (Cassidy, 2011, Williams and Talbot, 2011, Cheah et al., 2012, Shihadeh and Eissenberg, 2013).

No Sidestream Smoke (Geen passief roken)
Even though there is no sidestream smoke, there is exhaled breath. ‘Passive vaping’ occurs instead of ‘second-hand smoking’ given that measurements of indoor air after using an e-cigarette show the presence of formaldehyde (a known human carcinogen), acetaldehyde (a possible human carcinogen), and other volatile organic compounds (Schripp et al., 2013). Even e-liquids with 0 mg/ml nicotine (reported by manufacturer) showed levels of formaldehyde and acetaldehyde in indoor air after using the e-cigarette (Schripp et al., 2013).

Safe use for pregnant women
Nicotine crosses the placenta and is absorbed by the fetus. Nicotine can damage the fetal lungs, heart, and central nervous system (DKFZ, 2013).

Propylene glycol is Generally Regarded as Safe (GRAS) by the US FDA and therefore is safe
Propylene glycol is used in the food industry, as a food additive, as a solvent for food colours, flavours, pharmaceuticals, cosmetics, and in the paint and plastics industries. Propylene glycol is also used to create artificial smoke or mist during fire-fighting trainings, in discotheques, and in movie, television, and theatre productions (HCN, 2007). The US FDA has approved propylene glycol as GRAS for use as a direct food additive, for the use in cosmetics and a solvent in pharmaceuticals under certain conditions. The safety of inhalation of large concentrations of propylene glycol needs to be evaluated.

In general, a 300 puff e-cigarette is equivalent to 2 packs of cigarettes and a 500-puff e-cigarette is equivalent to 3 packs of conventional cigarettes.
Studies on human smoking behaviour show that smokers generally take approximately 13 puffs per cigarette (Djordjevic et al., 2000). A pack of 19 cigarettes would result in approximately 247 puffs.

Are e-cigarettes safe?
More research is needed to answer this question. The current main concerns are:
• Batteries, atomizers, cartridges, cartridge wrappers, packs and instruction manuals lack important information regarding e-cigarette content, use and essential warnings;
• E-cigarettes may contain toxic substances including diethylene glycol (a highly toxic substance), various nitrosamines (powerful carcinogens found in tobacco), and other chemicals suspected of being harmful to humans;
• Some e-cigarette cartridges labeled as containing no nicotine have nicotine present;
• The presence of carcinogens as a result of ‘passive vaping’ in indoor air;
• By simulating the cigarette experience, e-cigarettes might re activate the habit in ex-smokers. They could also be a gateway into tobacco abuse for young people who are not yet hooked;
• If e-cigarette cartridges with high levels of nicotine leak, they can expose nicotine, an addictive and dangerous chemical, to children, adults, pets and the environment;
• Currently, there are no methods for proper disposal of e-cigarette products and accessories, including cartridges, which could result in nicotine contamination from discarded cartridges entering water sources and soil, and adversely impacting the environment;
• The manufacture, quality control, sales, and advertisement of e-cigarettes are unregulated.
References


