Australian Government
Department of Health
National Industrial Chemicals Notification and Assessment Scheme

Non-nicotine liquids for e-cigarette devices in Australia: chemistry and health concerns

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1 Purpose and scope of this report

In light of limited publicly available information about the chemistry of liquids used in e-cigarette devices in Australia, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) has researched the chemicals used for this purpose in Australia and prepared this report.

The report does not contain a risk assessment of the chemicals identified as being present in e-cigarette liquids. The information in the report is available for use by risk managers as appropriate.

The aims of the report are to:

1. Identify the chemicals used in e-cigarette liquids available in Australia as well as the chemicals produced during e-cigarette use.
2. Describe chemical exposure from e-cigarette use, including potential differences arising from different types of devices and patterns of use.
3. Summarise possible human health concerns related to the chemistry of e-cigarette devices and liquids.
4. Ascertain the regulatory status of chemicals in e-cigarette liquids and chemicals produced by e-cigarettes during use.

Terms used in this report:

- *health concern* is used where there is evidence of a chemical hazard, but insufficient evidence to determine if there is likely to be a risk to human health from exposure to that chemical through e-cigarette use.
- *health effect* is used where there a reasonable level of evidence in the scientific literature that there is a risk to human health from exposure to a chemical through e-cigarette use.

2 Summary and key findings

This report considers:

- Chemicals to which people may be exposed from the use of e-cigarettes.
- The health concerns about these chemicals.

The key findings of this report are:

- The results of chemical analysis of e-cigarette devices and emissions available in Australia commissioned by the Australian Competition and Consumer Commission (ACCC) were consistent with other reports in the scientific literature.
- Many of the e-cigarette devices and liquids used in Australia are also available in other countries. There is no evidence that the e-cigarette liquids produced in Australia are substantially different from those found overseas.

- Therefore, this report assumes that overseas chemical and exposure information obtained from publicly available, scientifically rigorous reports of e-cigarette devices and liquids are directly applicable to those available in Australia.
- E-cigarette devices with higher power settings, mouth to lung (MTL) vaping, and dripping and squonking vaping may significantly increase chemical exposure relative to other e-cigarette use scenarios.
- There were 243 chemicals identified from published scientific literature as ingredients used in e-cigarette liquids, of which 235 were flavouring chemicals. It is likely there are other flavouring chemicals that have yet to be identified as ingredients used in e-cigarette liquids.
- Many flavours of e-cigarette liquids are available and the specific e-cigarette liquid used is a major determinant of the chemical exposure from e-cigarette use.
- A number of flavouring chemicals used as ingredients in e-cigarette liquids are of concern to human health. Of particular concern are diketone flavourings, which have been linked to irreversible lung damage known as bronchiolitis obliterans or 'popcorn lung'.
- Emissions from e-cigarette devices contain carbonyl compounds formed as reaction products of the e-cigarette liquid used, and these compounds may pose a risk to human health. Although it is uncertain as to whether some concentrations of carbonyl compounds measured in laboratory studies accurately reflect normal e-cigarette use, e-cigarette devices are capable of producing carbonyl compounds at levels that may be of concern to human health.
- E-cigarette emissions also contain contaminants mostly derived from the e-cigarette liquid but also from the device. The contaminants identified are metals, volatile organic compounds (VOC), phthalates, pesticides and tobacco-specific nitrosamines. At a sufficient concentration and exposure, the contaminants identified in e-cigarette emissions may have the potential to adversely affect human health.
- The particulate characteristics of e-cigarette emissions and modelling of their lung distribution indicate there is significant deposition of these emissions in the alveoli.
- E-cigarette use can cause acute (short-term) adverse health effects (to which nicotine may be a contributing factor), although the chronic (long-term) effects of e-cigarette use on health are unknown.

3 Regulation of e-cigarette liquids in Australia

3.1 Non-nicotine containing e-cigarette liquids

These types of liquids sold in Australia are for general consumer end-use. The chemicals used in them are subject to regulation as **industrial chemicals**. NICNAS assesses the human health and environmental risks of industrial chemicals in Australia, publishes information and makes recommendations to promote their safe use.

3.2 Nicotine-containing e-cigarette liquids

These types of liquids are not currently legally available for sale in Australia. The Therapeutic Goods Administration (TGA) regulates the use of nicotine in Australia in therapeutic goods and through access restrictions via the Poisons Standard.

4 Issues outside the scope of this report

The health concerns surrounding e-cigarette use are complex, and some issues are outside the scope of this report including:

- Specific health effects of exposure to nicotine through e-cigarette use.
- Health concerns about e-cigarette use not directly related to the hazards of chemicals in e-cigarette liquids and chemicals produced during use, such as explosion or burn hazards arising from malfunctioning e-cigarette devices.

5 Background information on e-cigarettes

E-cigarettes are electronic devices that use battery power to heat liquid to produce an inhalable emission that users commonly call a 'vapour'. They are also known as electronic cigarettes, electronic nicotine delivery systems (ENDS), electronic non-nicotine delivery systems (ENNDS), personal vaporisers, and vapes. The common term to describe the use of these devices is 'vaping'. They first became commercially available in 2004 and have significantly increased in popularity in the past few years (Rom et al. 2015).

E-cigarette use is particularly popular among current and former cigarette smokers. One reason for this is that the action of inhaling the emission from an e-cigarette device is similar to smoking conventional cigarettes or a water-pipe. The inhaled emission from e-cigarettes will contain nicotine only if nicotine is an ingredient in the e-cigarette liquid.

Although operating on the same general principle, e-cigarette devices vary considerably in form and functionality depending on the:

- intended vaping style
- preferred appearance
- sensory perception of the emission

- reusability
- e-cigarette liquid capacity
- power capacity
- ability to adjust power settings.

The ingredients of the liquids used in these devices are of particular interest in relation to chemical exposure. They can include flavouring chemicals, solvent chemicals such as glycerol and propylene glycol in varying proportions and, in some cases, nicotine. As noted previously, nicotine-containing liquids cannot be sold legally in Australia, although their sale is legal in some other countries.

There are 2 types of e-cigarette liquids in use based on the manufacturing process:

1. E-cigarette liquids are most commonly produced by mixing flavour concentrates with a vehicle (a liquid in which the flavours are dissolved).
2. Less common are **naturally extracted tobacco (NET) liquids**. NET liquids use flavouring obtained from the solvent extraction of tobacco (Farsalinos et al. 2015). NET liquids are marketed at various nicotine strengths including no nicotine, and intended for use in the same manner as other e-cigarette liquids. They are different from heated tobacco products.

As well as intentionally included ingredients, e-cigarette liquids and their inhaled emissions may also contain contaminants and reaction products. Reaction products are produced when the chemicals present in e-cigarette liquids and emissions react with light, heat or other chemicals. They are produced particularly when e-cigarette devices are heated to produce the inhalable emission.

While the risk from e-cigarettes use in relation to conventional cigarette smoking is currently under investigation, the use of e-cigarettes is not without concern to human health. E-cigarette users are exposed to chemicals:

- present in e-cigarette liquids
- produced during use
- used to make the device, which can contaminate the inhalable emissions.

Many of these chemicals can be harmful to human health in certain situations. There are peer-reviewed reports in the scientific literature providing evidence that e-cigarette use has short-term effects on human health. The exposure of e-cigarette users to such chemicals is of potential long-term human health concern.

6 Information sources used

The following sources of data were included in our analysis:

- Information on e-cigarette related commerce was obtained from Australian Customs data.
- Online vendors were identified using internet searches.
- Online vendor websites were used to identify a selection of e-cigarette devices and liquids used in Australia.
- General internet searches were conducted as required to identify relevant background information. This information was often in the form of advice or opinions from the e-cigarette user community. User experiences were helpful as some aspects of e-cigarette use can be highly technical, for example mechanical customisation of e-cigarette devices. There are also some activities and terminology that are exclusive to the e-cigarette user community.
- Chemical analysis of the emissions from e-cigarettes available in Australia commissioned by the Australian Competition and Consumer Commission (ACCC).
- Systematic reviews and reviews conducted partially in accordance with systematic review methodology were used to define evidence-based health effects from chemical exposure during e-cigarette use. Systematic reviews are carefully designed research studies. They use published information on a topic to investigate a specific question on that topic. These reviews are defined so that, if repeated, the same findings will be made for the research question examined. Systematic reviews comprise a relatively minor portion of the scientific literature on e-cigarettes. Relevant systematic reviews that addressed the other aims of this report were not available.
- Other peer-reviewed scientific literature on e-cigarettes

The peer-reviewed scientific literature considered included original research and review articles examining:

- Chemicals present in e-cigarette liquids and in the emissions from e-cigarette devices.
- Particles present in e-cigarette device emissions.
- Effect of different use patterns or types of e-cigarette devices on chemical exposure.
- Health concerns related to chemical exposure from e-cigarette use.
- Particular attention was given to reports specific to e-cigarettes and their use in Australia.

Any publications acknowledging assistance or a previous or current affiliation with industry associations or companies with an interest in e-cigarettes, tobacco, flavourings or tobacco cessation products have been marked as such in the reference list at the end of this document.

7 Vendors of e-cigarette devices in Australia and the devices and liquids sold

7.1 Analysis of Customs data related to import of e-cigarette devices and liquids

Customs import transactions from January 2016 to April 2018 were queried using the search terms, 'vape', 'vaping' and 'e-juice'. The results were filtered to remove entries either not importing e-cigarette related items or if the item being imported was uncertain. Using this search strategy, 156 introduction transactions from 35 unique introducers were identified. Using internet searches, an attempt was made to associate the companies identified with a web address. Although successful in a number of instances, the strength of the association between an importer and the web address varies. An example of a weak association is a close similarity between a business name in the Customs data and the name of a web address. An example of a strong link is the postal address in the Customs entry also being posted on the associated website. With this approach, likely websites were identified for 17 of the 35 introducers. It is likely that a significant proportion of e-cigarette device and liquid imports into Australia are not represented in this analysis. For example, introductions for personal use with a low value are not captured in Customs import data.

7.2 Identification of a representative selection of Australian online vendors

The scientific literature describes a telephone survey of e-cigarette users conducted in 2014 and 2015 in New South Wales (Australia). It identified internet sources as the most commonly used vendors for obtaining e-cigarettes and related items (Dunlop et al. 2016). Therefore, in May 2018, NICNAS conducted an internet search in order to identify online vendors likely to supply the Australian market. The internet search engines Google and Bing were used to identify Australian online retailers using the following parameters:

- The search terms used were 'e juice' and 'e liquid'
- The search term 'e-cigarette' was not used because most of the results for this term were for advocacy rather than vendor websites
- Search results were limited to those from Australia
- Vendors were identified from the first two pages of search results
- Location-specific results provided by Google were ignored as they would not appear if the search was conducted in another location
- Retailers advertising nicotine-containing e-cigarette liquids were also excluded as they probably represent an overseas supplier shipping directly to customers in Australia

Table 1 lists the online retailers identified using internet searching. Six (6) of the online retailers were identified using both search engines and some of the retailers were also identified in the analysis of Customs data.

Table 1: Online retailers of e-cigarette items identified through internet searching

Online retailer	Search engine that identified retailer
supervapestore.com.au	Google and Bing
www.juicewhore.com.au	Google and Bing
www.thebongshop.com.au	Google and Bing
smokemart.com.au	Google and Bing
vapestreet.com.au	Google and Bing
www.thevapestore.com.au	Google and Bing
www.victoryvape.com.au	Google
houseofvape.com.au	Google
www.vapecave.com.au	Google
www.vapetrain.com.au	Google
www.oz-eliquid.com.au	Google
www.vapesonline.com.au	Bing
www.sydneyvapesupply.com.au	Bing
www.steelcityvapor.com.au	Bing
www.aladdinsden.com.au	Bing
mrvapes.com.au	Bing
vapesquare.com.au	Bing
www.vaperempire.com.au	Bing
www.vapingmad.com.au	Bing
www.ecigworld.com.au	Bing
jostechecig.com.au	Bing
sociallites.com.au	Bing
www.wickandwireco.com.au	Bing

7.3 E-cigarette devices and liquids available from a selection of Australian online vendors

In July 2018, available e-cigarette items were documented from the 6 websites found using both Google and Bing searches described previously. Two (2) distinct types of items were noted from these websites:

- the first type of item was e-cigarette devices
- the second type of item was the liquids used in these devices.

Table 2 lists the brands of e-cigarette devices available from these websites.

Table 2: E-cigarette device brands available from websites identified from internet searches

Device Brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Aspire	✓	✓	✓	✗	✗	✗
Council of Vapor	✓	✗	✗	✗	✗	✗
Digiflavor	✗	✓	✗	✗	✗	✗
Eleaf	✓	✓	✓	✓	✗	✗
Flowermate	✓	✗	✗	✗	✗	✗
Geekvape	✓	✓	✓	✗	✗	✗
Ijoy	✓	✓	✓	✗	✗	✗
Innokin	✓	✓	✓	✓	✗	✗
Jomotech	✗	✗	✗	✗	✓	✗
Joyetech	✓	✓	✓	✗	✓	✗
KangerTech	✓	✓	✗	✓	✓	✓
Lost Vape	✓	✗	✗	✗	✗	✗
Sigelei	✓	✗	✗	✗	✗	✗
Smoant	✗	✗	✓	✗	✗	✗
Smok	✓	✓	✓	✗	✓	✗
Smokjoy	✗	✓	✗	✗	✗	✗
Teslacigs	✓	✗	✗	✗	✗	✗

Device Brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Uwell	✓	×	✓	×	×	×
Vandy Vape	✓	×	×	×	×	×
Vaporesso	✓	✓	✓	×	×	×
VGOD	✓	×	×	×	×	×
Vision	×	×	×	✓	×	×
VooPoo	×	✓	×	×	×	×
Wismec	✓	✓	✓	×	×	×

Complete website addresses for the websites listed in the table:

A. supervapestore.com.au
B. vapestreet.com.au
C. www.thevapestore.com.au
D. www.juicewhore.com.au
E. smokemart.com.au
F. www.thebongshop.com.au

For each of the brands listed in Table 2, there was at least 1 and usually more than 1 distinct device or model. The e-cigarette models predominantly marketed on the websites investigated were modular kits with a varying capacity for user customisation. The number of models offered within each brand varied from a single model to several models. Up to 18 models were available from the brand Smok across all of the websites inspected. Not all models within a brand were available across all of the websites. For example, within the brand Kangertech:

- the model Spider was only available from Super Vape Store and Smokemart
- the model Togo Mini was only available from Vape Street and The Bong Shop

The models available are designed for a number of different styles of vaping. For example within the brand Innokin, the AMVS Starter kit is intended for direct-to-lung vaping, while the Endura T18 is intended for mouth-to-lung vaping. The differences between these styles of vaping are discussed later in this report. E-cigarette devices require ongoing maintenance and the websites also offered replacement parts as well as parts for user customisation of e-cigarette devices. From further investigation of the brand, when the company's primary location was disclosed, their location was found to be predominantly in China, although a single US-based company was also identified. Counterfeiting may be a significant problem for e-cigarette device manufacturers as authenticity verification links are clearly visible on the landing pages of many of the device websites. The e-cigarette brands listed in Table 2 are also available in countries other than Australia, such as the USA. The availability of these devices in other countries suggests that:

- the use of certain e-cigarette devices in Australia is comparable to that in other countries and
- sources of information on e-cigarette devices from other countries are also directly applicable to Australia.

None of the 6 websites offered either disposable e-cigarette devices or prefilled cartridges containing e-cigarette liquid. However, the websites examined were not exhaustive, and Australian online vendors for these items are easily found by conducting simple internet searches. For example, sociallites.com.au provides cartridges and e-shisha.com.au provides disposable e-cigarettes.

Regarding the availability of e-cigarette liquids, all of the websites investigated offered ready-to-use e-cigarette liquids. Super Vape Store, Juice Whore and The Bong Shop additionally offered concentrates for e-cigarette users to create their own customised flavour combinations. Table 3 lists the brands of flavour concentrates intended for mixing that were available from these websites.

Table 3: E-cigarette liquid flavour concentrate brands available from websites

Flavour Conc. Brand	Websites		
	Super Vape Store[A]	Juice Whore[B]	The Bong Shop[C]
Capella Flavours	✓	✓	×
Flavour Art Australia	✓	✓	×
JW Signature	×	✓	×
Liquid Bam	✓	×	×
Super Vape Store	✓	×	×
The Flavor Apprentice	✓	✓	×
Tasty Puff Flavor Drops	×	×	✓

Complete website addresses for the websites listed in the table:

A. supervapestore.com.au
B. www.juicewhore.com.au

C. www.thebongshop.com.au

Many e-cigarette users do not create their own e-cigarette liquids by mixing concentrates, and the following brands of ready-to-use liquids were available from more than one of the websites investigated. Brands manufactured in Australia are also specified in the list below:

- Anarchist E-liquids
- Bogan Brews (manufactured in Australia)
- Botany Bay Bottling Co. (manufactured in Australia)
- Byron Bay Cloud Co. (manufactured in Australia)
- Candy King
- Cosmic Fog
- Dinner Lady
- Jam Monster
- Koncept XIX
- Nimbus Vapour (manufactured in Australia)
- Outerworld (manufactured in Australia)
- Stickyfingers (manufactured in Australia)
- That's My Jam (manufactured in Australia)
- The Milkman
- Twelve Monkeys
- Vagabond Vapour (manufactured in Australia)
- Vape Monster (manufactured in Australia)

The ready-to-use e-cigarette liquids identified from the websites investigated are listed in Table A1 in the Appendix. Many of the brands available from Australian online vendors investigated are also manufactured in Australia. The most common place of manufacture in website descriptions for e-cigarette liquids are Australia, USA and the UK. Common e-cigarette liquid flavours on these websites can be categorised as tobacco, fruit, cooling, dessert, and beverage. These e-cigarette liquids were also claimed to not contain nicotine.

In January 2014, a USA-based research group identified 466 brands of e-cigarettes with 7764 unique flavours. This represented a net increase in the number of brands and flavours available compared to 17 months earlier (Zhu et al. 2014). From the relatively small sample of Australian online vendors queried by NICNAS, 74 distinct brands were identified with the majority of these brands having more than 1 flavour. Australian e-cigarette users are also able to purchase e-cigarette liquids from vendors in other countries. Therefore, it is likely that there are hundreds to thousands of unique flavoured e-cigarette liquids available to a user in Australia. Do-it-yourself (DIY) descriptions for the manufacture of e-cigarette liquids outline a relatively simple process in which the desired mixture of flavouring chemicals is added to a solvent base and then packaged. Ingredient information provided by manufacturers and independent chemical analysis of e-cigarette liquids by numerous research groups indicates that commercially available e-cigarette liquids are also predominantly composed of a mixture of flavouring chemicals in a solvent base. A difference between e-cigarette liquids reported in the scientific literature and e-cigarette liquids legally available for sale in Australia is that the former often contains nicotine while the latter does not. There is no evidence that the presence or absence of nicotine affects the chemistry of non-nicotine chemicals present in e-cigarette liquid. However, it may be possible for nicotine to undergo reactions in e-cigarette liquids to generate additional chemicals not present in liquids without nicotine. Considering the concentration and reactivity of nicotine, any such reactions are unlikely to substantially alter the chemical composition of e-cigarette liquids. Other than nicotine, no country or region-specific differences in the composition of e-cigarette liquids have been noted. Therefore, chemical information obtained from nicotine-containing e-cigarette liquids is also applicable to liquids without nicotine, although consideration should be given to potential confounding chemical effects of nicotine.

7.4 Reports specific to Australia on e-cigarette use

There are a number of reports describing the prevalence and patterns of e-cigarette use in Australia or in certain regions of Australia. The National Drug Strategy Household Survey (NDSHS) is conducted every 2-3 years and collects information for the general population in Australia on alcohol, tobacco and other drug use. The 2016 survey report (The Australian Institute of Health and Welfare (AIHW) 2017) indicated that:

- 1.2% of people aged ≥ 14 used e-cigarettes
- E-cigarette use was most common in smokers aged 18-24
- 31% of smokers had tried e-cigarettes in their lifetime
- 4.4% of smokers use e-cigarettes with 1.5% of smokers using them daily
- 1.2% of ex-smokers use e-cigarettes and 0.6% of never smokers use e-cigarettes
- Younger smokers are more likely to have tried or currently use e-cigarettes

The NSW Ministry of Health conducted a telephone based survey in 2014 that included information on e-cigarette use from 12,502 respondents from NSW aged ≥ 18 years. Prevalence of e-cigarette use was 1.3% with 8.4% of the population having tried e-cigarettes, and smokers were more likely to be e-cigarette users than non-smokers. Males and persons aged 18-44 were also more likely to have tried an e-cigarette (Harrold et al. 2015).

Participants aged 12 to 17 (n = 4,277) in the Victorian section of the Australian Secondary Students' Alcohol and Drug (ASSAD) survey were queried regarding e-cigarette use. The prevalence of ever having used e-cigarettes was 14%, and 3% had used an e-cigarette within the past month. Most participants who had used e-cigarettes had also used conventional cigarettes (Williams and White 2018).

In an online survey of 3,188 NSW residents aged ≥ 18 years, 13% had tried an e-cigarette, 4.4% had used one in the past 30 days, and 0.6% reported daily use for the past 30 days. Younger people, current and ex-smokers, males, people with lower levels of education and people with lower incomes were more likely to have tried e-cigarettes than other corresponding groups. The most common reasons given for use were to help quit smoking or reduce the amount of traditional cigarettes smoked for current and ex-smokers. For non-smokers, the most common reasons given were novelty and the availability of different flavours. The most common enclosed places for e-cigarette use were the home (59.4%), workplace (27.8%) and the car (24.5%) (Twyman et al. 2018).

The product preferences of Australian young adult (18 to 25 years of age) e-cigarette users were examined through an online survey. Participants (n = 104) had an average age of 21.1 years, 57% were male, and 25%, 33%, 21% and 21% respectively reported using e-cigarettes daily, weekly, fortnightly and monthly. There was a preference for nicotine containing e-cigarette liquids (64%) over non-nicotine liquids in all users, which was more pronounced in smokers (71% preferring nicotine liquids) compared to non-smokers (56% preferring nicotine liquids) or never smokers (55% preferring nicotine liquids). These e-cigarette users also preferred flavoured (89%) over unflavoured (11%) e-cigarette liquids. Of those who preferred flavoured e-cigarette liquids, the most popular flavours (Jongenelis et al. 2018) were:

- 55% fruit flavours (e.g. apple, strawberry)
- 12% candy (e.g. bubble-gum, chocolate)
- 10% dessert (e.g. apple pie, vanilla)
- 10% mint
- 5% beverage (e.g. energy drink, coffee)
- 4% tobacco
- 3% menthol.

8 Impact of e-cigarette devices and patterns of use on chemical exposure

8.1 E-cigarette device type

E-cigarette devices operate by heating e-cigarette liquid to produce an inhalable emission, consisting primarily of aerosolised e-cigarette liquid. Generally, e-cigarette liquid is heated by a metallic coil using battery power. Coil temperatures of 145 to 334 °C have been reported under normal use conditions for an e-cigarette device (Chen et al. 2018). E-cigarette liquid is usually supplied to the coil by cotton or silica wicks, but other types of wicks are occasionally used. Apart from these general characteristics, the form that e-cigarette devices take varies considerably. They vary between:

- devices without any setting options, which are discarded after the single-use e-cigarette liquid reservoir has been depleted and
- complex devices with customisable components and settings that offer a high level of control of the user experience.

The range of different e-cigarette devices and the popularity of customising them create a very large number of potential chemical exposure scenarios. However, as described below, certain e-cigarette device features or characteristics that vary across devices can affect chemical exposure in a consistent manner.

Chemical exposure from e-cigarette devices is linked to power output of the device and the temperature of the heated coil. In addition to the electrical resistance of the coil, temperature is also affected by power supplied to the coil and the amount of e-cigarette liquid in the wick (Chen, W et al. 2018). An increase in the relative power supplied to an e-cigarette device can increase coil temperature, e-cigarette liquid consumption and corresponding emission mass. It can also increase the production of free radicals, carbonyl compounds and benzene (Bitzer, Goel, Reilly, Foulds, et al. 2018; Chen, W et al. 2018; Farsalinos, Poulas, and Voudris 2017; Farsalinos et al. 2018; Farsalinos et al. 2017; Geiss, Bianchi, and Barrero-Moreno 2016; Gillman et al. 2016; Kosmider et al. 2014; Ogunwale et al. 2017; Pankow et al. 2017; Sleiman et al. 2016). Increasing the power of variable power devices can also increase the concentration of certain metals in e-cigarette emissions (Zhao et al. 2019). A relatively small increase in device power has been shown to increase the production of carbonyl compounds. This is evidenced by increased carbonyl production occurring at power increments of less than 2 watts (W) and at device settings below 15 W (Farsalinos et al. 2017; Geiss, Bianchi, and Barrero-Moreno 2016; Gillman et al. 2016; Ogunwale et al. 2017). Carbonyl compounds present in e-cigarette emissions also increase with increasing coil temperature, with the production of these compounds rising steeply at temperatures above 350°C (Flora et al. 2017).

The power output capability of e-cigarette devices varies considerably. Simpler e-cigarette devices often have a maximum power output of up to approximately 15 W, while more complex high-end devices can deliver up to 350 W. Higher powered devices are generally intended for coils requiring more power to heat and may have features to prevent overheating of the coil. Nevertheless, there is still the potential for increased chemical exposure from the use of devices with high power outputs. High power devices tend to have a larger battery capacity and therefore also present a greater hazard in the case of a battery explosion.

Also related to coil temperature is the phenomenon known by e-cigarette users as dry puff. This is where an inadequate supply of e-cigarette liquid to the heating coils results in an unpleasant inhalation experience. In addition to the unpleasant sensation, dry puffs may also increase exposure to hazardous chemicals. Dry puff conditions result in a significant increase in the amount of formaldehyde present in the e-cigarette emission (Farsalinos et al. 2017). There is debate in scientific literature about whether levels of carbonyl compounds of concern to human health are produced not only under dry puff conditions but also under normal use (Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Pankow, Strongin, and Peyton 2015b, 2015a; Salamanca et al. 2018). Certain device designs, such as the heating coil being located at the top of the aerosolising component, are more likely to result in dry puff conditions (Gillman et al. 2016). Therefore, the susceptibility of specific devices to dry puffs is 1 factor that may impact on chemical exposure.

The chemical composition of an e-cigarette device can affect chemical exposure. A comparison was made of lead concentrations in e-cigarette liquids recovered from disposable e-cigarette devices to liquids that had not been in contact with a device. Findings suggest lead contamination of the liquids can occur as a result of contact with device components (Dunbar et al. 2018). Metals were found at higher concentrations in e-cigarette liquid recovered from the storage tank of e-cigarette devices and in corresponding e-cigarette emissions when compared to the freshly dispensed liquid. This suggests the transfer of metals from the device into the liquid and emissions (Olmedo et al. 2018). A particular concern for e-cigarette devices is the potential for metal from the heating coil to transfer into e-cigarette emissions leading to metal exposure during e-cigarette use (Hess et al. 2017; Olmedo et al. 2018; Williams et al. 2017). Alloys commonly used in e-cigarette heating coils are Kanthal, Nichrome, Stainless Steel, Nickel 200 and Titanium. Nickel is a known sensitiser and carcinogen, but potential nickel exposure from the use of coils containing high levels of nickel (Nichrome and Nickel 200) is yet to be investigated.

8.2 Patterns of e-cigarette device use

8.2.1 Mouth-to-lung and direct-to-lung vaping styles

Two common styles of vaping are mouth-to-lung (MTL) and direct-to-lung (DTL) vaping (Korzun et al. 2018).

In MTL vaping, the emission is sucked into the mouth and held for a relatively short period of time, before being inhaled into the lungs and then exhaled. This inhalation and exhalation pattern is similar to the pattern for conventional cigarette smoking. It is usually the intended vaping style for devices that operate with coil resistances of 1 ohm (Ω) and above and at lower wattages. Because of the similarity to cigarette smoking, MTL vaping may appeal to current, quitting and former smokers.

DTL puffing involves inhaling the emission directly into the lungs and then exhaling, which is a pattern similar to that used to smoke a water pipe. Devices used for DTL vaping tend to operate at higher power settings and use coils with resistances below 1 Ω. DTL puffs can produce relatively large aerosol formations when exhaled, and is popular with users aiming to produce large 'clouds', known in the user community as 'cloud chasing'. As the volume of the lungs is much greater than the volume of the mouth, the exposure to e-cigarette emission per puff is much greater for DTL than MTL vaping. This is supported by the fact that:

- for DTL vaping, it is advised to use approximately a quarter of the concentration of nicotine used for MTL vaping in order to prevent nicotine intoxication and
- DTL vapours tend to consume significantly more e-cigarette liquid than MTL vapours

E-cigarette device airflow is also higher for DTL than MTL puffing. Differences in airflow affect the formation of carbonyl compounds, and increased airflow also increases the consumption of e-cigarette liquid (Korzun et al. 2018). The production of volatile aldehydes from MTL and DTL e-cigarette devices was examined. For a particular device (either MTL or DTL), aldehyde production increased as the power increased. However, high powered DTL devices did not necessarily produce more aldehydes than lower powered MTL devices (Talih et al. 2017).

8.2.2 Dripping or squonking vaping styles

Dripping or squonking is another use pattern where extra liquid is provided to the coil by physically saturating the wick prior to a puff or small group of puffs. Saturating the wick can be achieved by:

- dripping, which is applying e-cigarette liquid directly to the coil assembly
- squonking, where an inbuilt squeeze bottle is used to mechanically administer liquid to the coil assembly

A coil temperature of up to 350°C was observed in a dripping e-cigarette device. The quantity of carbonyl reaction products in the emissions from this device was significantly greater than reported for other device types, comparable to the amount in traditional combustible cigarette smoke (Talih et al. 2016). However, these findings need to be confirmed across a range of similar devices before any firm conclusions can be drawn regarding chemical exposure from this use pattern.

9 Chemicals in e-cigarette devices and those produced during use

9.1 Scientific literature searches and determining chemical identity

The scientific literature was searched up to a publication date of July 2018, using PubMed for reports that provided information on the chemicals present in e-cigarette liquids and emissions. The concentration of chemicals, if stated in the report, was also collated. The chemicals identified were assigned to a category by NICNAS that reflected their origin, which were:

- ingredient, or
- reaction product, or
- contaminant.

A chemical was assigned to 1 of these categories based on the weighted consideration of all available sources of information, including the scientific literature and relevant information available from commercial organisations.

The Chemical Abstract Services (CAS) identity of chemicals was determined from either:

- A CAS descriptor provided in the report for that chemical.
- An appropriate CAS descriptor as determined by NICNAS based on the chemical name provided in the report.

If the CAS identity could not be established with reasonable certainty for a chemical described in a report, that chemical was not included.

9.2 Limitations for the chemicals identified from the scientific literature

There are certain limitations for the chemicals identified by NICNAS from the scientific literature.

When determining the origin of a chemical, in most cases the appropriate category as described in section 9.1 was clearly evident. In particular, many chemicals considered as flavouring compounds (ingredient category) were identified as such in the scientific literature and also by other sources such as chemical identity databases. However, occasionally a chemical could potentially be placed in more than 1 category. For example, acetaldehyde is described in scientific literature as a carbonyl reaction product formed during e-cigarette use, but also by other sources as a flavouring ingredient used in food products. In such situations, based on all the available information, a scientifically justified decision was made on the most likely category for the chemical.

NICNAS has not conducted further investigations to independently validate the descriptions provided in the scientific literature on:

- Purpose and/or source of chemicals

- Identity of chemicals
- Maximum concentration of chemicals in e-cigarette liquids or emissions.

It is possible that some of the information in the scientific literature on chemicals present in e-cigarette liquids and emissions may be inaccurate.

9.3 Chemical ingredients identified in e-cigarette liquids

The chemicals identified by NICNAS from the scientific literature are listed in Tables A2 to A6 of the Appendix along with the maximum reported concentration, and are grouped as:

- Table A2: Chemical Ingredients in E-cigarette Liquids
- Table A3: Chemical Contaminants in E-cigarette Liquids
- Table A4: Chemical Ingredients in E-cigarette Emissions
- Table A5: Chemical Reaction Products in E-cigarette Emissions Formed During E-cigarette Use
- Table A6: Chemical Contaminants in E-cigarette Emissions.

E-cigarette devices deliver chemicals present in e-cigarette liquid to the user in the form of an emission. Consequently, the chemicals present in the specific liquid used are a major determinant of chemical exposure during e-cigarette use. The liquids used in e-cigarette devices come in thousands of individual flavour varieties, and these flavours can be grouped as (Krusemann et al. 2018):

- tobacco
- menthol/mint
- nuts
- spices
- coffee/tea
- alcohol
- other beverages
- fruit
- dessert
- candy
- other sweets
- other flavours.

E-cigarette liquids are also available in unflavoured forms. However most e-cigarette liquids are flavoured and each flavour contains multiple flavouring chemicals. The majority of e-cigarette liquid ingredients identified by NICNAS from the scientific literature are used for the purpose of flavouring.

In total, NICNAS identified 243 different chemicals from a review of the published scientific literature as chemical ingredients used in e-cigarette liquids. These chemicals were identified either from analysis of e-cigarette liquids or emissions or from an analysis of both. Of these 243 chemicals, 235 were flavouring compounds and 8 had a purpose other than flavouring. Table A2 and Table A4 list the chemicals. A breakdown of the data summarising information sources and function of the chemicals is provided in Table 4. For chemicals identified only from analysis of e-cigarette liquids, 160 chemicals had an ingredient function and, of these, 156 were flavouring ingredients, with the remaining 4 chemicals having another purpose. Many ingredient chemicals were also identified from the analysis of e-cigarette emissions. An additional 19 flavouring ingredients not reported in e-cigarette liquids were identified from the analysis of e-cigarette emissions. As flavouring compounds are usually added to e-cigarette liquids as intentional ingredients these chemicals are likely to be present in e-cigarette liquids. Sixty four (64) chemical ingredients were identified from the analysis of both e-cigarette liquids and emissions. Of the ingredients identified from both emissions and liquids, 4 were for a purpose other than imparting flavour and the remainder were flavouring chemicals.

Table 4: Number, type and source of chemical ingredients identified from the scientific literature

	Ingredient function		
Source of information	**Flavouring**	**Other**	**Flavouring + Other**
Identified only in liquids	156	4	160
Identified only in emissions	19	0	19
Identified in both liquids and emissions	60	4	64
Total	**235**	**8**	**243**

Information on the concentration of an ingredient in e-cigarette liquids was available for 153 of the 243 ingredients identified. Individual flavouring compounds are commonly reported as being present at levels of between 1 µg/mL (or µg/g) to 10 mg/mL (or mg/g) in e-cigarette liquid. The highest concentrations reported for individual flavouring compounds were 21 mg/mL benzaldehyde, 71 mg/g ethyl maltol, 77 mg/mL limonene, 22 mg/mL menthol, 25 mg/g methyl cyclopentenolone, and 33 mg/mL vanillin (Bitzer, Goel, Reilly, Elias, et al. 2018; Tierney et al. 2016; Vardavas et al. 2017). The sum of flavouring chemicals quantified in 25 different e-cigarette liquid samples ranged from 2.6 to 43.0 mg/mL (Tierney et al. 2016). DIY e-cigarette liquid recipes are readily available on the internet, and often specify combined flavouring concentrates at concentrations of 10% or more. This is consistent with the amounts of flavouring chemicals reported in the scientific literature.

E-cigarette liquids also contain inactive excipients which function as solvents for flavouring ingredients in liquid form, and when heated by the e-cigarette device produce the inhaled aerosol. All e-cigarette liquids use glycerol, propylene glycol or most commonly a mixture of both as excipient ingredients. Common ratios of these ingredients used in e-cigarette liquids are:

- 50% glycerol and 50% propylene glycol and
- 70% glycerol and 30% propylene glycol

E-cigarette liquid manufacturers and retailers do not commonly disclose the complete list of chemical ingredients used for specific flavoured e-cigarette liquids. However, one of the few available sources for complete ingredient lists for certain liquids are Safety Data Sheets (SDSs). Table 5 lists the chemicals identified from an SDS prepared by Shenzhen Hangsen Star Technology Co. Ltd for a pineapple flavoured essence intended for end-use in e-cigarette devices. This is provided as an example of the ingredients in an e-cigarette liquid. It should be noted that there are limitations to the use of such information. Specifically, this SDS provides a list of ingredients as stated by the manufacturer, and NICNAS has not independently verified the identity or concentration of chemicals listed. However, most of the listed chemicals have also been described in the scientific literature and their use appears to be consistent with these reports. This SDS illustrates the chemical profile of a relatively common flavour used in e-cigarette liquids. While this particular liquid is not necessarily available in Australia, similar liquids are and equivalent Australian liquids may have a similar chemical makeup. The description of this liquid as an essence suggests that it is mixed with other flavours or diluted before use in e-cigarette devices. There are 18 different flavouring compounds used to create this flavour.

Table 5: Chemical ingredients provided by Shenzhen Hangsen Star Technology Co., Ltd for a pineapple flavoured e-cigarette liquid essence

Chemical name	CAS number	% in liquid
Propylene glycol (vehicle)	57-55-6	68.66
Allyl caproate	123-68-2	5.94
Allyl cyclohexanepropionate*	2705-87-5	4.84
Ethyl maltol	4940-11-8	3.58
Isoamyl butyrate	106-27-4	2.91
Ethyl butyrate	105-54-4	2.63
Ethyl caproate	123-66-0	2.49
Limonene	138-86-3	2.44
Methyl 3-methylthiopropanoate*	13532-18-8	1.28

Chemical name	CAS number	% in liquid
Ethyl 3-methylthiopropionate*	13327-56-5	1.09
trans-Nerolidol*	40716-66-3	0.72
Geranyl butyrate	106-29-6	0.63
Dimethylbenzylcarbinol acetate*	151-05-3	0.62
γ-Nonalactone	104-61-0	0.50
Leaf alcohol	928-96-1	0.49
Nerolidol*	142-50-7	0.39
Allyl heptanoate*	142-19-8	0.34
Vanillin propylene glycol acetal*	68527-74-2	0.32
Vanillin	121-33-5	0.13

Chemical names marked with (*) were not identified as flavouring ingredients in the scientific literature collated for this report.

The number of e-cigarette liquids analysed for chemical composition and reported in the scientific literature represents only a fraction of those available to the public. In addition, the chemical analysis was targeted to specific chemicals of interest, and some of the flavouring and other chemicals present in the samples described in the various reports have not been identified. Therefore, it is reasonably likely that many more predominantly flavouring chemicals remain to be identified as ingredients of e-cigarette liquids.

Some chemicals present in e-cigarette liquids have biological effects, such as flavouring chemicals that activate taste receptors and nicotine that acts on the central nervous system and other organs. Other biologically active chemicals can also be administered using e-cigarette devices. The scientific literature reports caffeine and synthetic cannabinoids as ingredients of e-cigarette liquids (Lisko et al. 2017; Peace et al. 2017). There is no indication that e-cigarette liquids containing synthetic cannabinoids are specifically available or being used in Australia. Liquids containing synthetic cannabinoids are controlled as specified in the Poisons Standard under the entry for "SYNTHETIC CANNABINOMIMETICS" and any other relevant entries.

9.4 Regulatory compliance of ingredient chemicals with the Industrial Chemicals (Notification and Assessment) Act 1989

Table 6 lists the 15 flavouring chemicals identified from reports of the analysis of e-cigarette liquids and emissions, and which are not listed on the Australian Inventory of Chemical Substances (the Inventory). The remaining 228 ingredient chemicals are listed on the

Inventory. These chemicals are subject to introduction requirements specified in the Industrial Chemicals (Notification and Assessment) Act 1989 (the Act). These chemicals either require notification to and assessment by NICNAS or are required to be exempted from notification prior to import or manufacture in Australia.

In addition, the flavouring chemical limonene (CAS number 138-86-3) has been assessed by NICNAS as a Priority Existing Chemical (PEC), and is subject to secondary notification obligations under the Act. For chemicals assessed under the Act, if a chemical's introducer becomes aware of new hazard or use information that may change the risk it poses, they must inform NICNAS. NICNAS then determines whether the information warrants a reassessment of the chemical.

Table 6: Chemicals identified as ingredients of e-cigarette liquids in scientific literature and not on the Inventory

Chemical name	CAS number
p-Anisaldehyde propylene glycol acetal	6414-32-0
β-Bourbonene	5208-59-3
Cadalene	483-78-3
β-Cadinene	523-47-7
Cadinol	11070-72-7
Carane	554-59-6
1,3-Dioxolane, 2-butyl-4-methyl-	74094-60-3
Isovanillin	621-59-0
MDMB-FUBINACA	1715016-77-5
p-Menthane-1,2-diol	33669-76-0
γ-Muurolene	30021-74-0
Nonylcyclopropane	74663-85-7
Octadecanal	638-66-4
2-Phenyl-1,3-dioxan-5-ol	1708-40-3
Sabinene	3387-41-5

9.5 Chemical reaction products produced during e-cigarette use

In addition to flavouring ingredients in e-cigarette liquids, another source of exposure to chemicals from e-cigarette use is from reaction products found in e-cigarette emissions. NICNAS identified 27 chemicals in the scientific literature that are considered to be reaction products originating from the chemicals present in e-cigarette liquids (Table A5). Of these 27 chemicals, 15 of the chemicals have data on the amount present in e-cigarette emissions.

The chemicals identified are predominantly carbonyl compounds with health concerns reported for many of these chemicals from use of e-cigarettes. This is discussed in detail later in this report. For the chemical species quantified and expressed as weight per mL of e-cigarette liquid consumed, the reaction products observed at the highest concentrations in e-cigarette emissions are listed in Table 7. There is ongoing debate about whether the higher concentrations of reaction products reported in literature are representative of actual use conditions for e-cigarettes or are artefacts from sub-optimal experimental designs (Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Pankow, Strongin, and Peyton 2015b, 2015a; Salamanca et al. 2018).

Table 7: Maximum reported levels of reaction products in e-cigarette emissions

Chemical name	CAS number	Highest reported amount
Acetaldehyde	75-07-0	19.1 mg/g liquid
Acetone	67-64-1	1.4 mg/mL liquid
Acrolein	107-02-8	10 mg/g liquid
Allyl alcohol	107-18-6	820 µg/g liquid
Butanal	123-72-8	40 µg/g liquid
2-Butanone	78-93-3	1.9 mg/g liquid
Crotonaldehyde	4170-30-3	720 µg/g liquid
Formaldehyde	50-00-0	48 mg/g liquid
Glycidol	556-52-5	760 µg/g liquid
Glyoxal	107-22-2	150 µg/g liquid
Isobutyraldehyde	78-84-2	3.9 ng/mL liquid
Methacrolein	78-85-3	460 µg/g liquid
Methylglyoxal	78-98-8	180 µg/g liquid
Propanal	123-38-6	3.2 mg/g liquid
Valeraldehyde	110-62-3	530 µg/g liquid

Liquid refers to the amount of liquid consumed (g or mL) to generate the emission.

Chemical reactions involving glycol solvents (glycerol and propylene glycol) used in e-cigarette liquids result in the formation of carbonyl compounds in the emissions (Jensen, Strongin, and Peyton 2017; Klager et al. 2017). A proposed scheme for the generation of reaction products from glycerol and propylene glycol used as excipient ingredients in e-cigarette liquids is reproduced from the report by Klager et al. (2017) in Figure 1 below. Similar schemes have also been presented in other reports in the scientific literature (Sleiman et al. 2016).

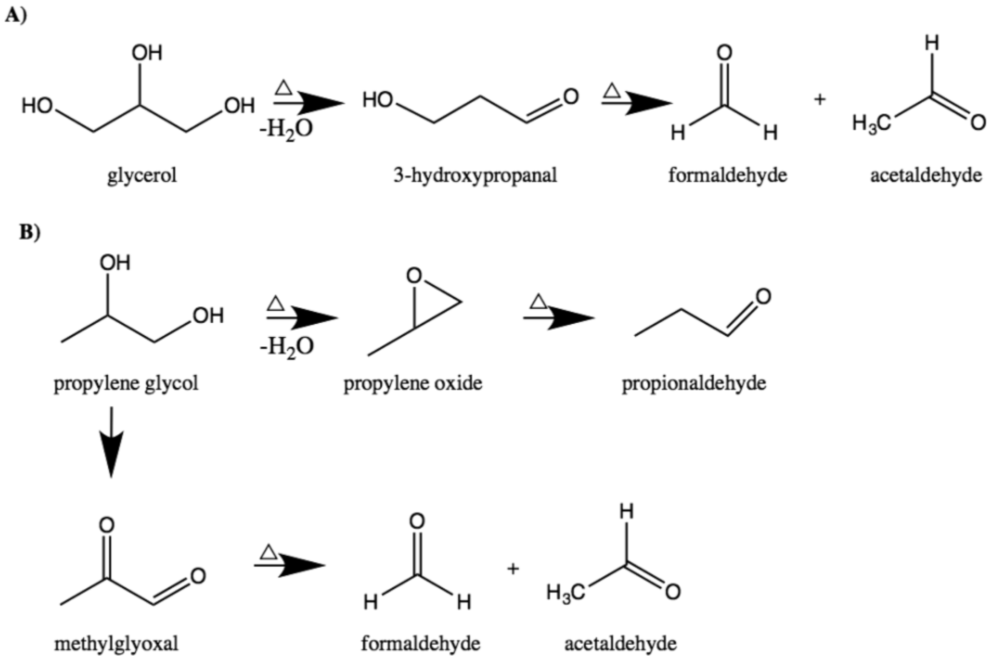

Figure 1: Proposed mechanisms of aldehyde formation from the pyrolysis and oxidation of (A) glycerol and (B) propylene glycol during emission formation from e-cigarette liquid (reproduced from Klager et al. 2017)

There is also limited evidence that flavouring chemicals used in these liquids may also contribute to the production of carbonyl reaction products (Fagan et al. 2017; Farsalinos and Voudris 2018; Khlystov and Samburova 2016; Klager et al. 2017).

Chemical ingredients used in e-cigarette liquids may react during storage of the liquid. The aldehyde flavouring chemicals benzaldehyde, cinnamaldehyde, citral, vanillin and ethylvanillin reacted with propylene glycol to produce acetal compounds over a period of 14 days (Erythropel et al. 2018). Other reactions involving flavouring chemicals may also occur. For example, this report has identified limonene as a common flavouring ingredient in many e-cigarette liquids (Table A2). In a separate risk assessment, NICNAS has also reported that limonene readily undergoes autoxidation when exposed to sunlight and air (National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2002). These observations are consistent with e-cigarette users who describe steeping e-liquids through ageing in order to develop the flavour of e-cigarette liquids for later use. Changes in the flavour of these liquids are expected to occur as a result of chemical reactions in the liquid.

NICNAS identified a total of 106 chemicals reported in scientific literature, that are considered as contaminants in both e-cigarette liquid and emissions. Tables A3 and A6 in the appendix lists each of these chemicals and a summary is provided below in Table 8. Of these chemicals, 52 were exclusively found in e-cigarette liquids, 25 exclusively in emissions, and 29 were identified in both liquids and emissions.

Many of the identified chemicals are volatile organic compounds (VOC), pesticides, metals and phthalates, with reported health concerns for some of the chemicals. Chemical concentrations were available for 59 of the 106 contaminants identified in e-cigarette liquids or emissions. Contaminants are usually present at much lower concentrations than intentional ingredients, often at concentrations below 1 µg/mL (0.0001%) in e-cigarette liquids. However, some contaminants are present at higher concentrations and comparable to intentional ingredients. For example, diethyl phthalate was reported at concentrations of up to 1.8 mg/mL (0.18%) and propylene oxide at up to 6.7 mg/mL (0.67%) in e-cigarette liquids (Oh and Shin 2015; Sleiman et al. 2016).

The presence of certain elemental contaminants in e-cigarette liquids and emissions, such as silicon and nickel, may originate from the components of the e-cigarette device rather than the e-cigarette liquid. In particular, there are a number of reports in literature examining the potential for metal exposure from the metal heating coils used in e-cigarette devices.

Table 8: Information source and number of chemical contaminants identified from the scientific literature

Information source	Number of chemicals
Identified only in liquids	52
Identified only in emissions	25
Identified in both liquids and emissions	29
Total	**106**

E-cigarette liquids are most commonly made by combining flavouring chemical mixtures with an appropriate solvent vehicle. Another less common method for producing e-cigarette liquids is by solvent extraction of tobacco leaves and then adding the extract to a vehicle. This type of e-cigarette liquid is known as naturally extracted tobacco (NET). NET e-cigarette liquids have not been as extensively examined and described in the literature, and the chemicals present in this type of liquid are less well defined than flavouring mixtures. Chemicals thus far identified in NET liquids are tobacco alkaloids and tobacco specific nitrosamines, which can be considered as contaminants.

9.6 Regulatory requirements for ingredient and contaminant chemicals with the Poisons Standard (SUSMP)

Table 9 lists chemicals identified by NICNAS from the scientific literature as ingredients and contaminants in e-cigarette liquids and which are also included in the schedules of the Poisons Standard (SUSMP). Products containing chemicals listed in Schedules 5 and 6 have certain labelling and packaging requirements, although the requirements for Schedules 5 and 6 do not apply if the concentration of the chemical does not exceed 10 mg per L or kg. Products containing chemicals in Schedule 7 should only be available to specialised or authorised persons in addition to having labelling and packaging requirements. Chemicals listed in Schedule 10 are prohibited in products as specified in the schedule.

Only schedule entries relevant to e-cigarettes are listed in Table 9. Some of the chemicals have additional schedule entries relating to other use patterns, such as medicinal use or specified use in products other than e-cigarettes, and these have not been included in the table. State and territory health authorities can be contacted for further information on the Poisons Standard.

Table 9: Chemicals from the scientific literature as present in e-cigarette liquids and also listed in the Poisons Standard

Chemical Name	CAS number	Entry Listed in Standard	Schedule	Amount Reported
Ingredient Chemicals				
Acetic acid	64-19-7	ACETIC ACID (excluding its salts and derivatives)	S5 if >30%, S6 if >80%	Not reported
Acetophenone	98-86-2	PHENYL METHYL KETONE	S5 if >25% (including other designated solvents)	5.7 µg/mL
1-Butanol	71-36-3	n-BUTYL ALCOHOL	S5 if >5%, S6 if >10%	10 µg/g
Butyl carbitol	112-34-5	DIETHYLENE GLYCOL MONOBUTYL ETHER	S5 if >10%	120 µg/mL
γ-Butyrolactone	**96-48-0**	**GAMMA BUTYROLACTONE (excluding its derivatives) in non-polymerised form**	**S10**	**41 µg/mL**
Camphor	76-22-2	CAMPHOR	S6 if >2.5%	1.3 mg/g
1,8-Cineol	470-82-6	CINEOLE	S6 if >25%	87 µg/g

Chemical Name	CAS number	Entry Listed in Standard	Schedule	Amount Reported
Ethylene glycol	**107-21-1**	**ETHYLENE GLYCOL (excluding its salts and derivatives)**	**S6 if >2.5%**	**76%**
Eugenol	97-53-0	EUGENOL	S6 if >25%	1.9 mg/mL
Furfural	98-01-1	FURFURAL	S6 if >0.1%	16 µg/mL
Methyl salicylate	119-36-8	METHYL SALICYLATE	S5 if >5%, S6 if >25%	76 µg/mL
Pulegone	89-82-7	D-PULEGONE	S6 if >4%	120 µg/g
Thujone	546-80-5	THUJONE	S6 if >4%	180 µg/mL
Contaminant Chemicals				
Acetone	67-64-1	ACETONE	S5 if >25% (including other designated solvents)	20 µg/g
Acrolein	**107-02-8**	**ACROLEIN**	**S7**	**10 ng/mL**
Antimony	NA	ANTIMONY COMPOUNDS	S6 if >1 mg per kg or L	1.5 ng/mL
Arsenic	NA	ARSENIC	S7 if >1 mg per kg or L	1.5 ng/mL
Benzene	71-43-2	BENZENE (excluding its derivatives)	S7 if >15 mL/L	2.3 µg/mL
Cadmium	NA	CADMIUM COMPOUNDS	S6	Not reported
Catechol	120-80-9	1,2-BENZENEDIOL	S6	1.7 µg/mL
Chlorpyrifos ethyl	2921-88-2	CHLORPYRIFOS	S5 if ≤5%, S6 if >5%	66 pg/mL
Copper	NA	COPPER COMPOUNDS	S6 if >5%	Not reported
m-Cresol	108-39-4	PHENOL, including cresols and xylenols and any other homologue of phenol boiling below 220°C	S6 if >3% (including other phenol homologues)	5.3 µg/mL

Chemical Name	CAS number	Entry Listed in Standard	Schedule	Amount Reported
o-Cresol	95-48-7	PHENOL, including cresols and xylenols and any other homologue of phenol boiling below 220°C	S6 if >3% (including other phenol homologues)	5.5 µg/mL
p-Cresol	106-44-5	PHENOL, including cresols and xylenols and any other homologue of phenol boiling below 220°C	S6 if >3% (including other phenol homologues)	1.0 µg/mL
Dichloromethane	75-09-2	DICHLOROMETHANE (methylene chloride)	S5	Not reported
Diethylene glycol	111-46-6	DIETHYLENE GLYCOL (excluding its salts and derivatives)	S6 if >2.5%	4 µg/g
Formaldehyde	50-00-0	FORMALDEHYDE (excluding its derivatives)	S6 if ≥0.05%	28 µg/mL
Lead	NA	LEAD COMPOUNDS	S6	838 ng/mL
Methanol	67-56-1	METHANOL (excluding its derivatives)	S5 if >2%, S6 if >10%	2.0 ng/mL
Methyl methacrylate	80-62-6	METHYL METHACRYLATE (excluding its derivatives)	S6	Not reported
Phenol	108-95-2	PHENOL, including cresols and xylenols and any other homologue of phenol boiling below 220°C	S6 if >1%	3.7 µg/mL
1-Propanol	71-23-8	n-PROPYL ALCOHOL	S5 if >5%, S6 if >10%	16 µg/g
Propylene oxide	**75-56-9**	**PROPYLENE OXIDE**	**S7**	**6.7 mg/mL**

Chemical Name	CAS number	Entry Listed in Standard	Schedule	Amount Reported
Propyl isocyanate	110-78-1	ISOCYANATES, free organic, boiling below 300° C	S6	Not reported
Styrene	100-42-5	STYRENE (excluding its derivatives)	S5	340 ng/mL
Toluene	108-88-3	HYDROCARBONS, LIQUID, including kerosene, diesel (distillate), mineral turpentine, white petroleum spirit, toluene, xylene and light mineral and paraffin oils (but excluding their derivatives); and TOLUENE (excluding its derivatives)	S5 if >25% (including other designated solvents), S6 if >50% toluene/xylene mixture	690 ng/mL
Xylene	1330-20-7	HYDROCARBONS, LIQUID, including kerosene, diesel (distillate), mineral turpentine, white petroleum spirit, toluene, xylene and light mineral and paraffin oils (but excluding their derivatives); and XYLENE (excluding its derivatives)	S5 if >25% (including other designated solvents), S6 if >50% xylene/toluene mixture	6.3 μg/mL

Additional Notes for Table 9:

- S5 refers to Schedule 5, S6 refers to Schedule 6, S7 refers to Schedule 7 and S10 refers to Schedule 10.
- Amount reported is the highest concentration of the chemical reported in e-cigarette liquids in scientific literature.
- Entries highlighted in bold were reported to be present in e-cigarette liquids at concentrations above the cut-offs for schedule entries relevant to e-cigarette liquids.

There were 38 chemicals identified from the scientific literature with listings in the Poisons Standard, of which 13 are likely ingredients and 25 are likely contaminants. One chemical, γ-butyrolactone (GBL) (CAS number 96-48-0) is listed in Schedule 10 and not permitted for use in e-cigarette liquids. This chemical is a prodrug (precursor and naturally converted in the body) for γ-hydroxybutyric acid (GHB) and is used as a recreational drug. However, GBL is also naturally present in certain flavours, and is described as a flavouring chemical by the Flavor and Extract Manufacturers Association of the United States (FEMA) with a flavour profile of caramel, cheese and roasted nut. Other chemicals described in the scientific literature at levels above cut-offs specified in the schedule (and relevant to e-cigarette liquids) are acrolein (CAS number 107-02-8) and propylene oxide (CAS number 75-56-9) in Schedule 7, and ethylene glycol (CAS number 107-21-1) in Schedule 6.

9.7 Chemical analysis of e-cigarette emissions and liquids commissioned by the Australian Competition and Consumer Commission (ACCC)

In 2016, the ACCC commissioned chemical analysis of e-cigarette emissions from 5 e-cigarette devices using a compatible liquid purchased in Australia. The 5 devices and liquid combinations tested as well as the vendor from which they were obtained are described in Table 10.

Table 10: E-cigarette devices and liquids tested for the ACCC, and their vendors

Vendor	Device	E-cigarette liquid
Ausvape	Vision Spinner II power supply and Kanger T3S tank	Ausvape
Elusion	Joyetech Ego kit	Elusion
eVape	Joyetech Ego kit	eVape
Joystick	Joystick branded device	Joystick
Social-Lites	Social-Lites branded device	Social-Lites

E-cigarette liquids were only analysed for nicotine, which was not found in any of the samples tested. No other chemicals in the e-cigarette liquids were analysed.

9.7.1 Analysis of emissions

To analyse e-cigarette emissions, an emission volume of 35 mL was collected at 1-minute intervals. For each e-cigarette device and liquid combination, two sampling protocols were utilised, which differed by the period of time over which samples were collected. The emissions were collected over either a 30 or 45-minute collection period. Chemical analysis of the emissions collected over the entire sampling period consisted of quantification of:

- Carbonyl compounds
- VOC, with certain species of VOC analysed semi-quantitatively
- Polycyclic aromatic hydrocarbons (PAH)
- Metals.

The CAS descriptors used in the ACCC commissioned reports were amended as necessary by NICNAS based on available information in a scientifically justified manner.

The carbonyl compounds acetaldehyde, acetone, acrolein, butanal, 2-butanone, crotonaldehyde, formaldehyde, and propanal were present in at least 1 of the samples analysed. Acetaldehyde, acrolein, butanal and formaldehyde were the most common carbonyl compounds identified and were present in emissions from all devices and liquids tested. All of these carbonyl compounds have also been described in the scientific literature as reaction products from e-cigarette device use. The relevance of the sampling conditions to realistic use conditions is unknown and was not addressed in the report. Nevertheless, as has been shown for e-cigarette devices purchased in other countries, e-cigarette devices available in Australia have the potential to expose users to hazardous chemical compounds.

VOC detected in the device emissions are listed in Table 11 and are present either from the intentional flavouring ingredients or as contaminants.

Table 11: VOCs other than carbonyl reaction products in e-cigarette device emissions analysed for the ACCC

Chemical	CAS number	Type of chemical	Also reported in literature
1,8-Cineol	470-82-6	Flavouring agent	Yes
Ethyl acetate	141-78-6	Flavouring agent	Yes
2-Ethyl-4-methyl-1,3-dioxolane	4359-46-0	Flavouring agent	No
p-Menthan-3-one	10458-14-7	Flavouring agent	No
Menthol	1490-04-6	Flavouring agent	Yes
α-Pinene	80-56-8	Flavouring agent	Yes
Triacetin	102-76-1	Flavouring agent	No
Benzoic acid	65-85-0	Contaminant	No
Bromoethane	74-96-4	Contaminant	No
Chloroethane	75-00-3	Contaminant	No
Dioxane	505-22-6	Contaminant	No
1,2-Dimethoxyethane (DME)	110-71-4	Contaminant	No
Ethyl carbazate	4114-31-2	Contaminant	No
Glyceryl 1-monoacetate	106-61-6	Contaminant	Yes
1-Methylglycerol	4435-50-1	Contaminant	No
1-Pentanol, 5-methoxy-	4799-62-6	Contaminant	No
Propene	115-07-1	Contaminant	No

The only metal found in the emissions from the devices and liquids tested was nickel, which was present in 4 of the 5 test sample combinations. No PAHs were detected in any of the emissions.

9.8 Chemical analysis of e-cigarette devices and liquids available in Australia reported in scientific literature

A recent report in the scientific literature describes chemical analysis of e-cigarette liquids sourced within Australia (Chivers et al. 2019). A total of 10 e-cigarette liquids comprising various brands and flavours were purchased within Australia from physical stores and online vendors. All liquids purchased were advertised as not containing nicotine. Chemicals present in the liquids were identified using gas chromatography mass spectrometry are described in Table 12.

Table 12: Chemicals identified from the analysis of 10 e-cigarette liquids purchased within Australia

Chemical	CAS number	Maximum concentration	Type of chemical	Reported in other literature
Glycerol and propylene glycol	56-81-5 and 57-55-6	99.5%	Excipient	Yes
Nicotine	54-11-5	0.29%	Ingredient	Yes
Anisaldehyde	123-11-5	-	Flavouring	Yes
Benzyl alcohol	100-51-6	-	Flavouring	Yes
Benzyl benzoate	120-51-4	-	Flavouring	Yes
Ethyl vanillin	121-32-4	-	Flavouring	Yes
Glycine	56-40-6	-	Flavouring	No
Isoeugenol	97-54-1	-	Flavouring	No
Menthol	1490-04-6	-	Flavouring	Yes
Triacetin	102-76-1	-	Flavouring	No
Vanillin	121-33-5	-	Flavouring	Yes
Hexadecanoic acid	57-10-3	1.7%	Contaminant	No
1-Methylglycerol	4435-50-1	0.18%	Contaminant	No
Octadecanoic acid	57-11-4	0.2%	Contaminant	No
Octanoic acid, 2-amino-	644-90-6	-	Contaminant	No
Phenol, 2-chloro-	95-57-8	0.47%	Contaminant	No
Propanoic acid	79-09-4	-	Contaminant	No

Chemical	CAS number	Maximum concentration	Type of chemical	Reported in other literature
Tetradecanoic acid	544-63-8	-	Contaminant	No

Nineteen (19) chemicals were identified from the analysis of e-cigarette liquids purchased in Australia. A further 7 chemicals could not be positively identified by the analysis. Of the chemicals identified, 12 were considered as ingredients with the remaining 7 considered as contaminants. Nine (9) of the 19 chemicals identified were also noted as present in e-cigarette liquids in the NICNAS review of the scientific literature.

10 Particulate matter from e-cigarette emissions and second-hand chemical exposure

Conventional cigarette smoke and e-cigarette emissions are primarily aerosols consisting of small particles suspended in the air, although a small portion may also exist in the gaseous phase. There are various ways a person can be exposed to either smoke or emissions, and terminology used to describe conventional cigarette smoke can also be used for e-cigarette emissions.

10.1 First hand and second hand e-cigarette emissions

First-hand e-cigarette emissions are produced by activating an e-cigarette to produce the aerosol that is intentionally inhaled by the user into the lungs. Once the first-hand emission is exhaled by the user it is considered a mainstream emission or second-hand emission. Conventional cigarettes also produce side-stream smoke from the burning end of the cigarette, which is a significant contributor to second-hand smoke. E-cigarette devices differ from conventional cigarettes by producing negligible amounts of side-stream emissions.

Second-hand e-cigarette emissions or cigarette smoke can then be inhaled by either the user or other people in the vicinity, which is known as passive vaping or passive smoking. There are a number of reports in scientific literature describing particulate matter (PM) in the first-hand and second-hand emissions from e-cigarette devices. Due to their small size, these particles can stay suspended in air for long periods of time. When inhaled, the size of the particle determines the primary site of deposition in the lungs, and smaller particles are more likely to deposit deeper within the respiratory tract. Particles with a diameter of up to 10 µm (PM_{10}) tend to deposit in the upper respiratory tract and large airways. Particles with diameters less than 2.5 µm ($PM_{2.5}$) in the small airways and alveoli, and diameters less than 0.1 µm ($PM_{0.1}$) in the alveoli (Guarnieri and Balmes 2014). At nanoscale dimensions, 10 µm, 2.5 µm and 0.1 µm are equal to 10,000 nm, 2,5000 nm and 100 nm respectively.

10.2 E-cigarette particulates reported in the scientific literature

Emissions from a 4-second puff from both disposable and reusable e-cigarette devices contained approximately 3×10^9 particles·per cubic centimetre (cm^{-3}). Puff durations of between 2 and 4 seconds the particles had an average diameter of between 272 and 458 nm. Both particle numbers and the average size of particles were similar to those observed with traditional combustible cigarettes (Ingebrethsen, Cole, and Alderman 2012). The distribution of emissions was characterised from both disposable and reusable e-cigarette devices using a 5-second puff. The number of particles in the 5 to 50 nm range was 10^7-10^8 particles·cm^{-3}, with a median diameter of 11-25 nm, and for particles in the 50 to 1000 nm range there were an equivalent number of particles with a median diameter of 96-175 nm (Mikheev et al. 2016). Nanoparticles and $PM_{2.5}$ were present in the emissions from a rechargeable e-cigarette device using tobacco and menthol flavoured e-cigarette liquid. The number of particles was higher in the tobacco-flavoured than menthol-flavoured liquid, suggesting the composition of the e-cigarette liquid may affect the particulate nature of the resulting emission (Lee et al. 2017). Emissions from a 2-second puff from an e-cigarette device using various e-cigarette liquids contained approximately 5×10^9 particles·cm^{-3} with median diameters of 107 to 165 nm. Deposition in the various regions of the lungs for these emissions was then estimated using computational models for estimating airway particle dosimetry. It was estimated that 7.7×10^{10} particles are deposited throughout the airways, more than double the estimate for conventional combustible cigarettes, and deposition was primarily in the alveoli (Manigrasso, Buonanno, Fuoco, et al. 2015; Manigrasso, Buonanno, Stabile, et al. 2015). The particulate characteristics of e-cigarette emissions along with dosimetry modelling suggest significant deposition of these emissions within the alveoli of the lungs.

A number of reports in the scientific literature report localised increases in atmospheric particulate matter and chemical contaminants as a result of e-cigarette use. In one report, higher indoor measurements of PM_{10}, $PM_{2.5}$ and $PM_{1.0}$ within a 45 m^3 room were described following a 2-hour e-cigarette use session undertaken by 3 persons (Schober et al. 2014). A separate study described that the indoor concentration of particulate matter (µg·m^{-3} of $PM_{1.0}$-PM_{10}) in a 50 m^3 room following e-cigarette use by a person was higher than background, but approximately 10-100 fold lower in comparison to smoking traditional combustible cigarettes (Ruprecht et al. 2014). In another study, the atmosphere was characterised in an environmentally controlled 30 m^3 chamber with an adapted cigarette smoking machine used to simulate e-cigarette use over 65-70 minutes. Propylene glycol, glycerol and nicotine but not carbonyl reaction products were detected in the air of the chamber. Particulate matter between 20 and 300 nm was collected within the chamber and reached a peak of 7×10^6 particles per litre (L^{-1}), while the concentration of particles >300 nm fell almost to baseline when actual e-cigarette use was stopped (Geiss et al. 2015). Another report described 3 persons using disposable or reusable e-cigarettes containing nicotine over a period of 2 hours in a 52.6 m^3 room shared with 6 non-users. Both $PM_{0.1}$ and $PM_{2.5}$ in the room increased following the use of either disposable or reusable e-cigarettes. Use of either type of e-cigarette also increased the amount of nicotine in the air and the nicotine deposited on surfaces or on the clothing of the non-users (Melstrom et al. 2017). In addition to the reports above describing second-hand emissions under defined laboratory conditions, there are also reports from real life settings during e-cigarette use. During an e-cigarette event held at a hotel, $PM_{2.5}$ increased from a baseline of <5 µg·per cubic metre (m^{-3}) to between 312 and 819 µg·m^{-3} in a 4023 m^3 event room containing between 50 and 100 e-cigarette users (Soule et al. 2017). A similar study investigated the air quality during an e-cigarette event in a 13,475 m^3 venue that contained an estimated 75 to 600 participants, depending on the time of day. PM_{10} increased from median background levels of 228 µg·m^{-3} to 11,327 µg·m^{-3} in the venue and VOC increased approximately 2-fold over background. The airborne concentration of nicotine during the event was an average of 125 µg·m^{-3}, which is equivalent to nightclubs and pubs that allow cigarette smoking (Chen et al. 2017). The persistence of chemicals in second hand e-cigarette emissions as suspended particulate matter and in the gaseous phase may result in additional chemical exposure through passive inhalation. Once the particles settle, there is also the potential for dermal exposure.

11 Health concerns from e-cigarette use

11.1 Health concerns from exposure to chemicals in e-cigarettes

11.1.1 Literature reports on nicotine-free e-cigarette liquids

Compared to studies of nicotine containing e-cigarette liquids, there are relatively few reports in the scientific literature investigating the health concerns from the use of nicotine-free liquids. Flavouring ingredients either alone, as ingredients of e-cigarette liquid mixtures, or obtained from e-cigarette emissions, and all without nicotine, are described as having adverse effects on the viability and function of various in vitro cell culture models (Behar et al. 2016; Bengalli et al. 2017; Cervellati et al. 2014; Clapp et al. 2017; Gerloff et al. 2017; Muthumalage et al. 2017; Sherwood and Boitano 2016; Ween et al. 2017). Nicotine-free e-cigarette liquids or their corresponding emissions have also been shown to have adverse effects on cell viability and function in oral and lung epithelial cell culture models (Sancilio et al. 2016; Sancilio et al. 2017; Schweitzer et al. 2015; Shen et al. 2016; Wu et al. 2014). There are a number of mouse studies in which pregnant mothers and neonatal pups were exposed to e-cigarette emissions without nicotine. Effects observed include inflammatory responses in the lungs of mothers and offspring and alterations in brain protein expression in offspring (Chen, H, Li, G, Chan, YL, Chapman, DG, et al. 2018; Chen, H, Li, G, Chan, YL, Nguyen, T, et al. 2018; Lauterstein et al. 2016; Zelikoff et al. 2018). Adult mice exposed to nicotine free e-cigarette emissions had impaired lung function and changes in gene expression in liver, kidney, muscle and brain (Larcombe et al. 2017; Lechasseur et al. 2017). Studies conducted on human subjects using e-cigarette devices and liquids without nicotine have also been reported. In human e-cigarette users inhaling nicotine-free emissions, no effects were observed on lung function, microcirculatory function, arterial stiffness, haemodynamic parameters, oxidative stress or cardiac sympathovagal balance (Chaumont et al. 2018a; Ferrari et al. 2015; Franzen et al. 2018; Moheimani et al. 2017). Subjects who occasionally smoked conventional cigarettes and with good tolerance to vaping (n=23) undertook either a MTL vaping session or a sham vaping session randomly 7 days apart. For the MTL session subjects took 25 puffs at a power setting of 60 W from an MTL e-cigarette device containing liquid comprised of 50% glycerol and 50% propylene glycol and no nicotine or flavouring chemicals. For the sham session subjects took 25 puffs from the same device setup but with device power turned off. Following MTL vaping sessions, endothelial microvascular function and oxidative stress remained unchanged. However, MTL vaping did induce acute tissue hypoxia, airway epithelial injury and small airway constriction (Chaumont et al. 2018b).

11.1.2 Other literature reports that may include nicotine

Due to the popularity of e-cigarette devices utilising nicotine overseas, in many studies of the health effects of e-cigarettes, nicotine is a component of the exposure scenario. While consideration of the specific effects of nicotine is outside the scope of this project, excluding studies that incorporate nicotine would considerably reduce the literature available for consideration. Therefore, to better characterise the health effects of e-cigarette use, studies with nicotine as a component of the liquids have been included, although it is noted that nicotine exposure may be a potential contributing factor to some of the effects discussed below. It is also noted that there are specific health concerns related to nicotine use in e-cigarette devices including acute toxicity, cardiovascular effects and effects on foetal development.

The National Academy of Sciences conducted a comprehensive scientific review to inform understanding of the public health impact of nicotine containing e-cigarette devices (National Academies of Sciences 2018). In conducting the review, the committee incorporated major attributes of formal systematic reviews. The Committee found that, in relation to human health effects, there is:

- Conclusive evidence that:
    - e-cigarette devices can explode and cause burns and projectile injuries
    - intentional or accidental exposure to e-liquids (from drinking, eye contact, or dermal contact) can result in adverse health effects including but not limited to seizures, anoxic brain injury, vomiting, and lactic acidosis. This is assumed to occur as a result of the acute toxicity of nicotine
    - intentionally or unintentionally drinking or injecting e-liquids can be fatal. This is assumed to occur as a result of the acute toxicity of nicotine.
- Substantial evidence that:
    - e-cigarette aerosols can induce acute endothelial cell dysfunction, although the consequences and outcomes on these parameters with long-term exposure to e-cigarette aerosol are uncertain
    - components of e-cigarette aerosols can promote formation of reactive oxygen species/oxidative stress. This supports the biological plausibility of tissue injury and disease from long-term exposure to e-cigarette aerosols
    - some chemicals present in e-cigarette aerosols (e.g. formaldehyde, acrolein) are capable of causing DNA damage and mutagenesis. This supports the biological plausibility that long-term exposure to e-cigarette aerosols could increase risk of cancer and adverse reproductive outcomes. Whether or not the levels of exposure are high enough to contribute to human carcinogenesis remains to be determined.
- Moderate evidence that:
    - e-cigarette use results in increased cough and wheeze in adolescents, and an association between e-cigarette use and an increase in asthma exacerbations.
- Limited evidence that:
    - e-cigarette use is associated with a short-term increase in systolic blood pressure, changes in biomarkers of oxidative stress, increased endothelial dysfunction and arterial stiffness, and autonomic control

- in vivo animal studies using intermediate biomarkers of cancer support the hypothesis that long-term e-cigarette use could increase the risk of cancer
- e-cigarette aerosol can be mutagenic or cause DNA damage in humans, animal models, and human cells in culture
- e-cigarette exposure results in adverse effects on the respiratory system from animal and in vitro studies
- nicotine and non-nicotine containing e-cigarette aerosol can adversely affect cell viability and cause cell damage of oral tissue in non-smokers

Other findings of the committee are outside the scope of the current work and are not described here, but can be found in the committee's original report. Another review found that the commonly reported adverse effects of e-cigarette use were cough, mouth or throat irritation, anxiety, depressed mood, nausea, and insomnia (Liu et al. 2018). Other systematic reviews did not draw any further conclusions regarding the health effects related to chemical exposure from e-cigarette use (Callahan-Lyon 2014; Glasser et al. 2017; Pisinger and Dossing 2014).

A retrospective analysis was conducted of calls to Australian Poisons Information Centres made between 2009 and 2016 (Wylie et al. 2019). The study reported that calls to Australian Poisons Information Centres regarding e-cigarette exposures increased substantially between 2012 and 2016. Of the calls reported, 38% were regarding children exposed to e-cigarette liquids, and the remaining 62% were in relation to the exposure of adolescents or adults. Adverse effects appear to be the result of nicotine present in e-cigarette liquids and are described as gastrointestinal disturbances and sedation. The report also notes the recent death of an infant in Australia from ingestion of nicotine containing liquid. Deaths due to acute nicotine toxicity have been reported in other countries from the ingestion of nicotine containing e-cigarette liquids (National Academies of Sciences 2018).

11.2 Recent human studies investigating health concerns from e-cigarette use

Scientific literature published between September 2017 and April 2019 was searched in PubMed for reports investigating health concerns from e-cigarette use in human subjects. Searches were not conducted for reports published prior to September 2017 since they were assumed to have been captured by the comprehensive review conducted by the National Academy of Sciences (National Academies of Sciences 2018).

Oral health was compared between former smokers (n = 45) and current e-cigarette users (n =45) in an observational study of dental clinic patients over a 2-year period. Oral mucosal lesions were more common in current e-cigarette users than former smokers, although the difference was not significant. However, nicotine stomatitis (inflammation of oral mucosa), hairy tongue and angular cheilitis (inflammation of the lips) were observed significantly more often in e-cigarette users (Bardellini et al. 2018).

COPDGene is a multicentre observational study aiming to identify genetic factors associated with chronic obstructive pulmonary disease (COPD). More than 10,000 smokers are enrolled in this study. E-cigarette use was associated with increased prevalence of chronic bronchitis and was also predictive of COPD exacerbations in a subset of 3536 COPDGene participants (Bowler et al. 2017).

The Behavioral Risk Factor Surveillance System (BRFSS) is an annual cross-sectional survey collecting data on health-related risk behaviours, chronic health conditions, and use of preventive services. In 8087 participants in the 2016 BRFSS conducted in Hawaii, e-cigarette use was associated with respiratory disorder independent of cigarette use and other physical and psychosocial covariates (Wills et al. 2019). Further, data from the 2016 and 2017 BRFSS were pooled and in the 449,092 participants there was no association between e-cigarette use and cardiovascular disease in individuals who had never smoked. However, persons who both smoked conventional cigarettes and also used e-cigarettes were more likely to have cardiovascular disease than those who only smoked conventional cigarettes (Osei et al. 2019).

The National Health Interview Survey (NHIS) is conducted by the U.S. Census Bureau by in-person interviews of randomly sampled persons 18 years and older regarding a broad range of health topics. In participants pooled from the 2014 and 2016 surveys (n = 69,452), daily e-cigarette use but not occasional or former e-cigarette use was associated with a higher risk of myocardial infarction (Alzahrani et al. 2018). It should be noted that the observational nature of the studies described above limits causal inference between e-cigarette use and the health status described.

11.3 Health concerns for flavouring compounds and other ingredients present in e-cigarette liquids

NICNAS has identified over 200 flavouring compounds in the scientific literature that are added intentionally to e-cigarette liquids to impart flavour. Often they are present at relatively high concentrations of 1% or greater. Three of these chemicals (CAS numbers 76-22-2, 108-39-4 and 97-53-0) are listed in the Poisons Standard relevant to e-cigarette use (see section 9.7). Some of these compounds have also been flagged in the scientific literature as having health concerns from e-cigarette use, summarised in Table 13. In particular, diketone flavourings are associated with permanent lung damage also known as popcorn lung, and other health concerns include respiratory irritation, sensitisation, acute toxicity, impaired cell function, and the potential to form harmful reaction products. The actual risk posed by these flavouring compounds to human health is still to be determined. The list of chemicals in Table 13 is not an exhaustive list of flavouring chemicals with health concerns related to e-cigarette use.

Table 13: List of flavouring compounds (non-exhaustive) in e-cigarettes with human health concerns

Chemical	CAS number	Concern	References
Acetoin	513-86-0	Irreversible lung damage, irritation	(Allen et al. 2016; Clapp and Jaspers 2017)
2-Acetylpyrazine	22047-25-2	Respiratory irritation	(Vardavas et al. 2017)
Acetylpropionyl	600-14-6	Irreversible lung damage, cytotoxicity, irritation	(Allen et al. 2016; Barhdadi et al. 2017; Clapp and Jaspers 2017; Farsalinos, Kistler, et al. 2015; Barrington-Trimis, Samet, and McConnell 2014; Holden and Hines 2016; LeBouf et al. 2018; Muthumalage et al. 2017)
Benzaldehyde	100-52-7	Irritation	(Clapp and Jaspers 2017; Kosmider et al. 2016; Tierney et al. 2016)
Camphor	76-22-2	Irritation	(Clapp and Jaspers 2017)
Cinnamaldehyde	104-55-2	Cytotoxicity, impaired immune cell function, sensitisation	(Behar et al. 2016; Clapp et al. 2017; Muthumalage et al. 2017)
m-Cresol	108-39-4	Irritation	(Clapp and Jaspers 2017)
α and β Damascone		Respiratory irritation, cytotoxicity	(Sherwood and Boitano 2016; Vardavas et al. 2017)
Diacteyl	431-03-8	Irreversible lung damage, irritation	(Allen et al. 2016; Barhdadi et al. 2017; Clapp and Jaspers 2017; Farsalinos, Kistler, et al. 2015; Barrington-Trimis, Samet, and

Chemical	CAS number	Concern	References
			McConnell 2014; Holden and Hines 2016; LeBouf et al. 2018)
2,5-Dimethylpyrazine	123-32-0	Respiratory irritation, impaired cell function	(Sherwood and Boitano 2016; Vardavas et al. 2017)
Ethyl caproate	123-66-0	Respiratory irritation	(Vardavas et al. 2017)
Ethyl maltol	4940-11-8	Respiratory irritation, cytotoxicity	(Sherwood and Boitano 2016; Vardavas et al. 2017)
Ethyl vanillin	121-32-4	Respiratory irritation	(Vardavas et al. 2017)
Eugenol	97-53-0	Sensitisation	(Clapp and Jaspers 2017)
α and β-Ionone		Respiratory irritation, cytotoxicity	(Sherwood and Boitano 2016; Vardavas et al. 2017)
Isopentyl acetate	123-92-2	Irritation	(Clapp and Jaspers 2017)
Limonene	138-86-3	Respiratory irritation	(Vardavas et al. 2017; LeBouf et al. 2018)
Linalol	78-70-6	Respiratory irritation, cytotoxicity	(Sherwood and Boitano 2016; Vardavas et al. 2017)
Menthol	1490-04-6	Respiratory irritation, cytotoxicity	(Clapp and Jaspers 2017; Willershausen et al. 2014; Vardavas et al. 2017)
Methyl cyclopentenolone	80-71-7	Respiratory irritation	(Vardavas et al. 2017)
α-Pinene	80-56-8	Irritation	(LeBouf et al. 2018)
Vanillin	121-33-5	Irritation, cytotoxicity, impaired cell function	(Muthumalage et al. 2017; Sherwood and Boitano 2016; Tierney et al. 2016)

Chemical	CAS number	Concern	References
Various Flavour Compounds		Cytotoxicity, impaired immune cell function, formation of hazardous free radicals and carbonyl compounds	(Bitzer, Goel, Reilly, Elias, et al. 2018; Khlystov and Samburova 2016; Leigh et al. 2016; Leslie et al. 2017; Muthumalage et al. 2017; Qu, Kim, and Szulejko 2018; Rowell et al. 2017; Ween et al. 2017)
Various Sweeteners		Formation of hazardous furans and carbonyl compounds	(Fagan et al. 2017; Soussy et al. 2016)
Veratraldehyde	120-14-9	Respiratory irritation	(Vardavas et al. 2017)

Certain flavourings used in e-cigarette liquids, including some of those identified as being of concern to health in Table 13, are designated as Generally Recognised as Safe (GRAS) as specified by the US Food and Drug Administration (US-FDA) for use as food additives. However, GRAS designation does not mean that a chemical is also safe for inhalation as a flavouring ingredient in e-cigarette liquid, a position that is supported by the Flavor and Extract Manufacturers Association of the United States (FEMA) (Flavor and Extract Manufacturers Association of the United States 2018). Further research is required to establish the safety of flavouring chemicals for use in e-cigarette liquids as exposure to these chemicals occurs through the inhalation route and there is a potential for the formation of reaction products during heating.

As noted previously, flavouring chemicals in e-cigarette liquids can form reaction products with propylene glycol during storage, and there are concerns that the chemical species produced may be harmful to human health (Erythropel et al. 2018). Limonene is commonly present in e-cigarette liquids, and NICNAS has previously identified the autoxidation products of limonene present a greater risk for sensitisation than limonene itself (National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2002). Also of concern is that excipient ingredients (glycerol and propylene glycol) may pose a hazard to human health from their use in e-cigarette liquids (Ghosh et al. 2018).

11.4 Health concerns for reaction products and contaminants in e-cigarette emissions

Carbonyl reaction products in e-cigarette emissions identified in the scientific literature as being of concern to human health include acetaldehyde, acetone, acrolein and formaldehyde. In particular, formaldehyde is the most frequently identified reaction product and is also usually present at the highest concentration in comparison to other reaction products. Hazardous properties that are of concern from inhalation exposure to formaldehyde during e-cigarette use are the potential for respiratory corrosion, sensitisation and carcinogenicity. Formaldehyde levels of up to 48 mg/g e-cigarette liquid consumed or 99 ng/mL of emission have been reported in emissions from e-cigarettes. However, the reported levels of carbonyl compounds including formaldehyde vary significantly between research groups. Some groups have reported concentrations comparable to or exceeding those expected from traditional combustible cigarette smoking, while other groups have reported levels marginally above ambient levels. There is ongoing discussion as to whether the experimental conditions in the studies that reported higher concentrations reflect realistic use of e-cigarette devices (Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Pankow, Strongin, and Peyton 2015b, 2015a; Salamanca et al. 2018). Therefore, at this point in time, the relevance of observed amounts of carbonyl compounds generated from e-cigarette devices to human health is uncertain. However, there is conclusive evidence that e-cigarette devices generate harmful carbonyl compounds. Accordingly, these devices are also capable but not necessarily likely to produce these compounds at levels that are of concern to human health.

A number of reports have also identified elemental metals in e-cigarette emissions, which often originate from the device components rather than the liquid. Metals identified that are of concern even at low exposure levels include arsenic, chromium, lead, mercury and nickel. Other chemical contaminants identified in e-cigarette emissions with the potential to adversely affect human health include phthalates, pesticides and VOC.

12 Reports by other Australian government agencies

The Commonwealth Scientific and Industrial Research Organisation (CSIRO) was commissioned by the Department of Industry, Innovation and Science to look at e-cigarettes and their effects on health (Byrne et al. 2018).

The report comprehensively reviewed the scientific literature on the effect of e-cigarette use on individual and population health and smoking rates when compared to conventional cigarette smoking. The key findings of the report were:

- Regular use of e-cigarettes is likely to have an adverse effect on health. However, there is a lack of clarity about the magnitude of adverse health effects, and the quantity of e-cigarette use required to trigger adverse health effects.
- Many e-cigarette users also often smoke conventional cigarettes.
- E-cigarette use by non-smoking youths may be predictive of future smoking in this group.
- The effectiveness of e-cigarettes as a smoking cessation method is unknown.

- Completely substituting e-cigarettes for conventional cigarettes may lead to an improvement in individual health. However, the use of e-cigarettes may introduce independent health risks.
- Currently it is not possible to determine whether improving accessibility to e-cigarettes would reduce smoking rates in Australia.

Australian Government Department of Health Policy Statements and Research

The policy position of the Department of Health to e-cigarettes in is detailed at the following website:

https://www.health.gov.au/resources/publications/principles-that-underpin-the-current-policy-and-regulatory-approach-to-e-cigarettes-in-australia

The National Health and Medical Research Council (NHMRC) has released a statement on the safety and efficacy of e-cigarettes that can be accessed at the following website:

https://www.nhmrc.gov.au/health-advice/all-topics/electronic-cigarettes

This site also contains information on the research on e-cigarettes funded by the NHMRC.

In addition, the Department of Health has commissioned the National Centre for Epidemiology and Population Health at the Australian National University (ANU) to conduct a public health assessment of e-cigarette use for the Australian context.

The public health assessment of e-cigarette use will inform decision-making by developing a framework to consider evidence on the likely risks and benefits of e-cigarettes. The final report is expected at the end of 2020.

Appendix

Appendix Table A1: Ready to use e-cigarette liquid brands advertised on websites identified from internet searches

E-cigarette liquid brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
24 K Vaping Co.	✓	×	×	×	×	×
888 Vapes Australia	✓	×	×	×	×	×
Adam Bomb	×	✓	×	×	×	×
Alpha Vape	×	✓	×	×	×	×
Anarchist E-liquids	✓	✓	×	×	×	×
Ant Hill	×	×	✓	×	×	×
Bad Drip Labs	✓	×	×	×	×	×
Banana Butt	×	✓	×	×	×	×
Big Daddy	✓	×	×	×	×	×
Black Note	✓	×	×	×	×	×
Blue Label	×	✓	×	×	×	×
BLVK Unicorn	×	✓	×	×	×	×
Bogan Brews	✓	×	✓	×	×	×
Bombshell Premium E-Liquid	✓	×	×	×	×	×
Botany Bay Bottling Co.	✓	×	✓	×	×	×
Bubble Gang	×	✓	×	×	×	×
Bunyip Vapes	✓	×	×	×	×	×
Byron Bay Cloud Co.	✓	✓	×	×	×	×
Cake Vapors	×	✓	×	×	×	×
Candy King	✓	✓	×	×	×	×
Charlie's Chalk Dust	×	×	×	×	✓	×

E-cigarette liquid brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Cloudy Days	✓	×	×	×	×	×
Cloud Mouth Vapors	✓	×	×	×	×	×
Clutch Vapors	×	✓	×	×	×	×
Cosmic Fog	✓	×	×	×	✓	×
Crisp	×	×	×	×	✓	×
Cuttwood Vapors	✓	×	×	×	×	×
Dainty's	×	×	×	×	✓	×
Dimension Vapour	×	×	✓	×	×	×
Dinner Lady	✓	✓	✓	×	×	×
Dirty Harry Collection	×	×	✓	×	×	×
Donuts	×	×	✓	×	×	×
Dr Picnic's Magic Elixir	×	✓	×	×	×	×
Electric Sky	×	✓	×	×	×	×
Famous Fair	×	✓	×	×	×	×
Fruit N Custard	×	✓	×	×	×	×
FRYD	×	✓	×	×	×	×
Grill'D	×	✓	×	×	×	×
Hemlock Vapor	×	✓	×	×	×	×
Humble Juice Co	×	✓	×	×	×	×
Jam Monster	✓	✓	×	×	×	×
Juice Whore	×	×	×	✓	×	×
Juicy Co	×	✓	×	×	×	×
Koncept XIX	✓	×	×	×	✓	×

E-cigarette liquid brand	**Websites**					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Liqua	✓	×	×	×	×	×
Liquid EFX Vape	✓	×	×	×	×	×
London Blend	×	×	×	×	✓	×
Mad Hatter Juice	✓	×	×	×	×	×
Mr Joph's Miracle Mist	×	×	✓	×	×	×
Mr Meringue	×	✓	×	×	×	×
Naked 100	✓	×	×	×	×	×
Nectar Nation	✓	×	×	×	×	×
Nimbus Vapour	✓	×	✓	×	×	×
O2	×	×	×	×	✓	×
One Hit Wonder	✓	×	×	×	×	×
One Off Co	✓	×	×	×	×	×
Outerworld	✓	✓	✓	×	×	×
Outrun Vape	✓	×	×	×	×	×
Pachamama	×	✓	×	×	×	×
Primal Elixirs	×	✓	×	×	×	×
Propaganda	✓	×	×	×	×	×
Psycho Bunny	×	×	×	×	✓	×
Ripe Vape	×	✓	×	×	×	×
Royale	×	×	×	×	✓	×
Savage	×	×	×	×	✓	×
Skwezed	×	✓	×	×	×	×
Silk Road Vapour	×	✓	×	×	×	×
Silverback Juice Co	✓	×	×	×	×	×

E-cigarette liquid brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Small Tobacco	×	✓	×	×	×	×
Spectral Vapour	✓	×	×	×	×	×
Sticky Fingers	✓	✓	×	×	×	×
Strange Fruit	×	✓	×	×	×	×
Strawberry Queen	×	✓	×	×	×	×
Sugoi Vapor	×	✓	×	×	×	×
Super Vape Store	✓	×	×	×	×	×
Sweet & Simple Vape Co	✓	×	×	×	×	×
Tasty Puff	×	×	×	×	×	✓
That's My Jam	✓	×	✓	×	×	×
The Collection Ejuices	×	✓	×	×	×	×
The Custard Shoppe	×	✓	×	×	×	×
The Milkman	✓	✓	×	×	×	×
The Vape Store	×	×	✓	×	×	×
Time Bomb	×	✓	×	×	×	×
Time Zone	×	✓	×	×	×	×
Twelve Monkeys	✓	✓	×	×	×	×
Vagabond Vapour	✓	×	✓	×	×	×
Vape Monster	✓	×	✓	×	×	×
Vape Monastery	✓	×	×	×	×	×
Vape Pink	✓	×	×	×	×	×
Vaper Treats	×	✓	×	×	×	×
Vapetasia	✓	×	×	×	×	×
Vapour Eyes	×	×	✓	×	×	×

E-cigarette liquid brand	Websites					
	Super Vape Store[A]	Vape Street[B]	The Vape Store[C]	Juice Whore[D]	Smoke Mart[E]	The Bong Shop[F]
Vapour Head	×	×	×	×	✓	×
Vanilla Vapes UK	✓	×	×	×	×	×
Yami Vapor	×	✓	×	×	×	×

Complete website addresses for the websites listed in the table:

A. supervapestore.com.au
B. vapestreet.com.au
C. www.thevapestore.com.au
D. www.juicewhore.com.au
E. smokemart.com.au
F. www.thebongshop.com.au

Appendix Table A2: Chemical ingredients in e-cigarette liquids

Chemical	CAS number	Maximum amount reported	Reference
Acetal	105-57-7	40 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Acetic acid	64-19-7		(Sleiman et al. 2016)
Acetoin	513-86-0	16 µg/g (Varlet et al. 2015)	(Allen et al. 2016; Varlet et al. 2015)
Acetophenone	98-86-2	5.7 µg/mL (Schober et al. 2014)	(Hutzler et al. 2014; Schober et al. 2014)
Acetovanillin	881-68-5	-	(Hutzler et al. 2014)
4-Acetylanisole	100-06-1	-	(Hutzler et al. 2014)
Acetylpropionyl (2,3-Pentanedione)	600-14-6	1.0 mg/mL (Farsalinos, Kistler, et al. 2015)	(Allen et al. 2016; Barhdadi et al. 2017; Farsalinos, Kistler, et al. 2015; LeBouf et al. 2018)

Chemical	CAS number	Maximum amount reported	Reference
2-Acetylpyrazine	22047-25-2	1.1 mg/mL (Vardavas et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Lim and Shin 2017; Vardavas et al. 2017)
2-Acetylpyridine	1122-62-9	340 µg/mL (Aszyk et al. 2018)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
2-Acetylpyrrole	1072-83-9	21 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Allyl caproate	123-68-2	-	(Hutzler et al. 2014)
Amyl alcohol	71-41-0	71 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Sleiman et al. 2016)
Amyl isovalerate	25415-62-7	-	(Peace et al. 2017)
Anethol	104-46-1	13 µg/mL (Schober et al. 2014)	(Geiss et al. 2015; Schober et al. 2014)
Anisaldehyde	123-11-5	9.6 µg/mL (Schober et al. 2014)	(Hutzler et al. 2014; Schober et al. 2014)
Anise alcohol	105-13-5		(Hutzler et al. 2014)
4-Anisyl acetate	104-21-2	61 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
p-Anisaldehyde propylene glycol acetal	6414-32-0	-	(Hutzler et al. 2014)
Benzaldehyde	100-52-7	21 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Tierney et al. 2016; Varlet et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Benzaldehyde propylene glycol acetal	2568-25-4	900 µg/mL (Tierney et al. 2016)	(Hutzler et al. 2014; Tierney et al. 2016)
Benzophenone	119-61-9	-	(Hutzler et al. 2014)
Benzyl acetate	140-11-4	1.2 mg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
Benzyl alcohol	100-51-6	8.4 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Schober et al. 2014; Sleiman et al. 2016; Tierney et al. 2016)
Benzyl benzoate	120-51-4	-	(Hutzler et al. 2014)
Benzyl cinnamate	103-41-3	-	(Hutzler et al. 2014)
Benzyl propionate	122-63-4	-	(Hutzler et al. 2014)
Benzyl salicylate	118-58-1	-	(Hutzler et al. 2014)
β-Bourbonene	5208-59-3	-	(Hutzler et al. 2014)
1-Butanol	71-36-3	10 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Butyl butyryllactate	7492-70-8	-	(Hutzler et al. 2014)
Butyl carbitol	112-34-5	120 µg/mL (Schober et al. 2014)	(Hutzler et al. 2014; Schober et al. 2014)
2-sec-Butyl-cyclohexanone	14765-30-1	-	(Hutzler et al. 2014)
Butyl hexadecanoate	111-06-8	-	(Eddingsaas et al. 2018)
Butyl octadecanoate	123-95-5	-	(Eddingsaas et al. 2018)
γ-Butyrolactone	96-48-0	41 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)

Chemical	CAS number	Maximum amount reported	Reference
Cadalene	483-78-3	-	(Geiss et al. 2015)
δ-Cadinene	483-76-1	-	(Geiss et al. 2015)
β-Cadinene	523-47-7	-	(Hutzler et al. 2014)
Caffeine	58-08-2	350 µg/g (Lisko et al. 2017)	(Lisko et al. 2017)
Camphor	76-22-2	1.3 mg/g (Lisko et al. 2015)	(Lisko et al. 2015; Schober et al. 2014)
α-Cedrene	469-61-4	-	(Geiss et al. 2015)
Capric acid	334-48-5	80 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018; Hutzler et al. 2014)
Carane	554-59-6	-	(Geiss et al. 2015; Hutzler et al. 2014)
Carvone	99-49-0	930 µg/mL (Aszyk et al. 2018)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Geiss et al. 2015; Hutzler et al. 2014; Sleiman et al. 2016; Tierney et al. 2016)
Caryophyllene	87-44-5	-	(Hutzler et al. 2014)
Caryophyllene oxide	1139-30-6	-	(Hutzler et al. 2014)
1,8-Cineol	470-82-6	87 µg/g (Lisko et al. 2015)	(Hutzler et al. 2014; Lisko et al. 2015; Sleiman et al. 2016)
Cinnamaldehyde	104-55-2	140 mg/mL (Behar et al. 2016)	(Behar et al. 2016; Eddingsaas et al. 2018; Hutzler et al. 2014; Lisko et al. 2015; Tierney et al. 2016)
Citral	5392-40-5	22 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Aszyk, Wozniak, et al. 2017; Bitzer, Goel, Reilly, Elias, et al. 2018; Hutzler et al. 2014)

Chemical	CAS number	Maximum amount reported	Reference
(R)-(+)-Citronellal	2385-77-5	-	(Hutzler et al. 2014)
Citronellol	106-22-9	23 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018; Aszyk et al. 2018)
Cocal	21834-92-4	36 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
Coumarin	91-64-5	-	(Hutzler et al. 2014)
Creosol	93-51-6	-	(Hutzler et al. 2014)
Cuparene	16982-00-6	-	(Geiss et al. 2015)
Damascenone	23696-85-7	-	(Hutzler et al. 2014)
α-Damascone	43052-87-5	78 µg/mL (Vardavas et al. 2017)	(Vardavas et al. 2017; Hutzler et al. 2014)
β-Damascone	23726-92-3	1.5 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Aszyk, Kubica, et al. 2017; Bitzer, Goel, Reilly, Elias, et al. 2018; Aszyk et al. 2018; Tierney et al. 2016; Vardavas et al. 2017)
α-Decalactone	18436-37-8	-	(Hutzler et al. 2014)
γ-Decalactone	706-14-9	8.2 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Bitzer, Goel, Reilly, Elias, et al. 2018; Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018; Aszyk et al. 2018; Hutzler et al. 2014)
δ-Decalactone	705-86-2	32 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018)
n-Decanal	112-31-2	150 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
Diacetin	25395-31-7	-	(Hutzler et al. 2014)

Chemical	CAS number	Maximum amount reported	Reference
Diacetyl (2,3-Butanedione)	431-03-8	11 mg/mL (Farsalinos, Kistler, et al. 2015)	(Allen et al. 2016; Barhdadi et al. 2017; Farsalinos, Kistler, et al. 2015; Varlet et al. 2015; LeBouf et al. 2018)
Diethyl malonate	105-53-3	-	(Hutzler et al. 2014)
Diethyl succinate	123-25-1	3.1 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Difurfuryl disulfide	4437-20-1	-	(Hutzler et al. 2014)
3,4-Dihydrocoumarin	119-84-6	72 µg/mL (Schober et al. 2014)	(Aszyk, Wozniak, et al. 2017; Hutzler et al. 2014; Schober et al. 2014)
p-Dimethoxybenzene	150-78-7	16 µg/mL (Schober et al. 2014)	(Schober et al. 2014)
(2,2-Dimethoxyethyl) benzene	101-48-4	-	(Hutzler et al. 2014)
α,α-Dimethylphenethyl butyrate	10094-34-5	500 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
2,6-Dimethylpyridine	108-48-5	57 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
2,5-Dimethylpyrazine	123-32-0	200 µg/mL (Vardavas et al. 2017)	(Aszyk, Kubica, et al. 2017; Vardavas et al. 2017)
1,3-Dioxolane, 2-butyl-4-methyl-	74094-60-3	-	(Geiss et al. 2015)
2,6-Di-tert-butyl-p-cresol	128-37-0	-	(Hutzler et al. 2014)
γ-Dodecalactone	2305-05-7	51 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Schober et al. 2014)
Dodecane	112-40-3	640 µg/mL (Oh and Shin 2015)	(Oh and Shin 2015)

Chemical	CAS number	Maximum amount reported	Reference
Elemol	639-99-6	-	(Hutzler et al. 2014)
Ethanol	64-17-5	25% (Peace et al. 2017)	(Lim and Shin 2017; Peace et al. 2017; Sleiman et al. 2016; Varlet et al. 2015; LeBouf et al. 2018)
Ethyl acetate	141-78-6	7.2 mg/mL (Tierney et al. 2016)	(Lim and Shin 2017; Tierney et al. 2016; Varlet et al. 2015)
Ethyl acetoacetate	141-97-9	15 mg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Hutzler et al. 2014)
Ethyl benzoate	93-89-0	-	(Hutzler et al. 2014)
Ethyl butyrate	105-54-4	11 mg/mL (Tierney et al. 2016)	(Aszyk et al. 2018; Peace et al. 2017; Tierney et al. 2016)
Ethyl caproate	123-66-0	550 µg/mL (Vardavas et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Vardavas et al. 2017)
Ethyl caprylate	106-32-1	-	(Hutzler et al. 2014)
Ethyl cinnamate	103-36-6	180 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018; Hutzler et al. 2014)
Ethylene glycol	107-21-1	76% (Hutzler et al. 2014)	(Hahn et al. 2014; Hutzler et al. 2014; Varlet et al. 2015)
Ethyl heptanoate	106-30-9	120 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018; Hutzler et al. 2014)
Ethyl hexadecanoate	628-97-7	-	(Hutzler et al. 2014)
2-Ethylhexyl fumarate	141-02-6	-	(Hutzler et al. 2014)
Ethyl 3-hydroxybutanoate	5405-41-4	-	(Peace et al. 2017)
Ethyl isovalerate	108-64-5	700 µg/mL (Tierney et al. 2016)	(Peace et al. 2017; Tierney et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Ethyl lactate	97-64-3	50 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
Ethyl nonanoate	123-29-5	-	(Hutzler et al. 2014)
Ethyl maltol	4940-11-8	71 mg/g (Vardavas et al. 2017)	(Aszyk, Kubica, et al. 2017; Bitzer, Goel, Reilly, Elias, et al. 2018; Eddingsaas et al. 2018; Aszyk et al. 2018; Geiss et al. 2015; Hutzler et al. 2014; Miao et al. 2016; Peace et al. 2017; Schober et al. 2014; Tierney et al. 2016; Vardavas et al. 2017)
Ethyl α-methylbutyrate	7452-79-1	-	(Hutzler et al. 2014)
Ethyl 3-methyl-3-phenylglycidate	77-83-8	300 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018; Hutzler et al. 2014)
Ethyl 2-methylpropanoate	97-62-1	86 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018)
Ethyl myristate	124-06-1	-	(Hutzler et al. 2014)
Ethyl phenylacetate	101-97-3	2.6 mg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Hutzler et al. 2014; Peace et al. 2017; Schober et al. 2014)
Ethyl propanoate	105-37-3	120 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Ethyl salicylate	118-61-6	13 µg/g (Lisko et al. 2015)	(Lisko et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Ethyl vanillin	121-32-4	9.1 mg/g (Vardavas et al. 2017)	(Aszyk, Kubica, et al. 2017; Bitzer, Goel, Reilly, Elias, et al. 2018; Eddingsaas et al. 2018; Aszyk et al. 2018; Hahn et al. 2014; Hutzler et al. 2014; Schober et al. 2014; Tierney et al. 2016; Vardavas et al. 2017)
Ethylvanillin propylene glycol acetal	68527-76-4	110 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Bitzer, Goel, Reilly, Elias, et al. 2018)
Eugenol	97-53-0	1.9 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
Folione	111-12-6	-	(Peace et al. 2017)
D-Fructose	57-48-7	330 µg/mL (Fagan et al. 2017)	(Fagan et al. 2017)
Furaneol	3658-77-3	7.6 mg/mL (Schober et al. 2014)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Schober et al. 2014)
Furfural	98-01-1	16 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
Furfuryl alcohol	98-00-0	45 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
Geranyl acetate	105-87-3	-	(Hutzler et al. 2014)
Geranyl butyrate	106-29-6	-	(Hutzler et al. 2014)
Geranyl propionate	105-90-8	60 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)

Chemical	CAS number	Maximum amount reported	Reference
D-Glucose	50-99-7	89 µg/mL (Fagan et al. 2017)	(Fagan et al. 2017)
Glutaric acid, dimethyl ester	1119-40-0	-	(Hutzler et al. 2014)
Glycerol	56-81-5	100% (Peace et al. 2016)	(Beauval et al. 2017; Eddingsaas et al. 2018; Etter and Bugey 2017; Geiss et al. 2015; Hahn et al. 2014; Hutzler et al. 2014; Peace et al. 2016; Peace et al. 2017; Schober et al. 2014; Sleiman et al. 2016)
Glyceryl monocaprate	26402-22-2	-	(Hutzler et al. 2014)
Hedione	24851-98-7	370 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014)
γ-Heptalactone	105-21-5		(Hutzler et al. 2014)
γ-Hexalactone	695-06-7	190 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Hexaldehyde	66-25-1	530 ng/g (Varlet et al. 2015)	(Varlet et al. 2015)
2,3-Hexanedione	3848-24-6	-	(LeBouf et al. 2018)
n-Hexanoic acid	142-62-1	-	(Hutzler et al. 2014)
1-Hexanol	111-27-3	1.6 mg/mL (Aszyk et al. 2018)	(Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018; Aszyk et al. 2018)
trans-2-Hexenol	928-95-0	4.5 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Tierney et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
3-Hexenyl acetate	1708-82-3	540 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
cis-3-Hexenyl acetate	3681-71-8	140 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018)
cis-3-Hexenyl valerate	35852-46-1	80 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
Hexyl acetate	142-92-7	2.5 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
α-Hexyl-cinnamaldehyde	101-86-0	-	(Hutzler et al. 2014)
Hexyl butanoate	2639-63-6	-	(Eddingsaas et al. 2018; Hutzler et al. 2014)
Hexyl hexanoate	6378-65-0	500 µg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Eddingsaas et al. 2018; Aszyk et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
Hydrocinnamic acid	501-52-0	-	(Peace et al. 2017)
Hydroxyacetone	116-09-6	7.7 mg/mL (Sleiman et al. 2016)	(Sleiman et al. 2016)
5-Hydroxymethylfurfurol	67-47-0	-	(Peace et al. 2017)
Ionone	8013-90-9	200 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Vardavas et al. 2017)
α-Irone	79-69-6	-	(Sleiman et al. 2016)
β-Irone	79-70-9	-	(Sleiman et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Isoamyl butyrate	106-27-4	290 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014)
Isoamyl isovalerate	659-70-1	490 µg/mL (Aszyk et al. 2018)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014)
Isobornyl acetate	125-12-2	-	(Hutzler et al. 2014)
Isobutyl acetate	110-19-0	26 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Isobutyl benzoate	120-50-3	-	(Hutzler et al. 2014)
Isomenthol	3623-52-7	-	(Hutzler et al. 2014)
Isomethyl-α-ionone	127-51-5	-	(Hutzler et al. 2014; Sleiman et al. 2016)
Isopentyl acetate	123-92-2	2.3 mg/mL (Aszyk et al. 2018)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
Isopentyl alcohol	123-51-3	-	(Sleiman et al. 2016)
Isopentyl isobutyrate	2050-01-3	-	(Hutzler et al. 2014)
2-Isopropyl-5-methyl-2-hexenal	35158-25-9	90 µg/mL (Aszyk et al. 2018)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
(-)-Isopulegol	89-79-2	-	(Geiss et al. 2015)
Isovanillin	621-59-0	-	(Peace et al. 2017)
Leaf alcohol	928-96-1	4.3 mg/mL (Tierney et al. 2016)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Oh and Shin 2015; Sleiman et al. 2016; Tierney et al. 2016)
Leaf aldehyde	6728-26-3	400 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)

Chemical	CAS number	Maximum amount reported	Reference
Limonene	138-86-3	77 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Bitzer, Goel, Reilly, Elias, et al. 2018; Aszyk, Wozniak, et al. 2017; Hutzler et al. 2014; Schober et al. 2014; Tierney et al. 2016; Vardavas et al. 2017; LeBouf et al. 2018)
Linalol	78-70-6	23 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Aszyk, Kubica, et al. 2017; Bitzer, Goel, Reilly, Elias, et al. 2018; Aszyk et al. 2018; Geiss et al. 2015; Hutzler et al. 2014; Peace et al. 2017; Sleiman et al. 2016; Vardavas et al. 2017)
Linalool oxide	1365-19-1	53 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Linalyl acetate	115-95-7	350 µg/mL (Aszyk et al. 2018)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
Maltol	118-71-8	6.2 mg/mL (Tierney et al. 2016)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
MDMB-FUBINACA	1715016-77-5	-	(Peace et al. 2017)
Melonal	106-72-9	84 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
p-Menthane-1,2-diol	33669-76-0	-	(Hutzler et al. 2014)

Chemical	CAS number	Maximum amount reported	Reference
Menthol	1490-04-6	22 mg/mL (Tierney et al. 2016)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Geiss et al. 2015; Hutzler et al. 2014; Lisko et al. 2015; Schober et al. 2014; Tierney et al. 2016; Vardavas et al. 2017)
Menthone	89-80-5	3.0 mg/mL (Aszyk et al. 2018)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Tierney et al. 2016)
Menthyl acetate	89-48-5	6.4 mg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Geiss et al. 2015)
Methyl acetate	79-20-9	-	(Hutzler et al. 2014)
4-Methyl acetophenone	122-00-9	67 µg/mL (Aszyk et al. 2018)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
Methyl anthranilate	134-20-3	1.3 mg/mL (Tierney et al. 2016)	(Peace et al. 2017; Tierney et al. 2016)
2-Methylbutyl acetate	624-41-9	900 µg/mL (Tierney et al. 2016)	(Tierney et al. 2016)
Methyl cinnamate	103-26-4	640 µg/mL (Oh and Shin 2015)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Oh and Shin 2015)
6-Methylcoumarin	92-48-8	-	(Hutzler et al. 2014)
3-Methyl-1,2-cyclopentanedione	765-70-8	-	(Hutzler et al. 2014)

Chemical	CAS number	Maximum amount reported	Reference
Methyl cyclopentenolone	80-71-7	25 mg/g (Vardavas et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Schober et al. 2014; Vardavas et al. 2017)
5-Methylfurfural	620-02-0	220 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
Methylheptenone	110-93-0	34 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Methyl 2-methylbutyrate	868-57-5	12 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
4-Methyl-2-pentyl-1,3-dioxolane	1599-49-1	-	(Hutzler et al. 2014)
2-Methylpyrazine	109-08-0	45 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
Methyl salicylate	119-36-8	76 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017)
γ-Muurolene	30021-74-0	-	(Geiss et al. 2015)
Neomenthol	3623-51-6	600 µg/mL (Tierney et al. 2016)	(Tierney et al. 2016)
γ-Nonalactone	104-61-0	370 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014)
Nonylcyclopropane	74663-85-7	-	(Hutzler et al. 2014)
Nootkanone	4674-50-4	-	(Hutzler et al. 2014)
γ-Octalactone	104-50-7	-	(Hutzler et al. 2014)
Phenethyl alcohol	60-12-8	430 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Schober et al. 2014)

Chemical	CAS number	Maximum amount reported	Reference
Phenethyl isovalerate	140-26-1	11 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
2-Phenyl-1,3-dioxan-5-ol	1708-40-3	-	(Hutzler et al. 2014)
α-Pinene	80-56-8	-	(LeBouf et al. 2018)
β-Pinene	127-91-3	2.5 µg/mL (Schober et al. 2014)	(Schober et al. 2014)
Piperitone	89-81-6	-	(Geiss et al. 2015; Hutzler et al. 2014)
Piperonal	120-57-0	7.5 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Bitzer, Goel, Reilly, Elias, et al. 2018; Eddingsaas et al. 2018; Hutzler et al. 2014; Tierney et al. 2016)
Piperonal propylene glycol acetal	61683-99-6	-	(Eddingsaas et al. 2018; Hutzler et al. 2014)
1,3-Propanediol	504-63-2	10% (Hahn et al. 2014)	(Hahn et al. 2014)
Propenylguaethol	94-86-0	-	(Hutzler et al. 2014)
Propylene glycol	57-55-6	100% (Peace et al. 2016)	(Beauval et al. 2017; Eddingsaas et al. 2018; Etter and Bugey 2017; Geiss et al. 2015; Hahn et al. 2014; Hutzler et al. 2014; Peace et al. 2016; Peace et al. 2017; Schober et al. 2014; Sleiman et al. 2016)
Pulegone	89-82-7	120 µg/g (Lisko et al. 2015)	(Geiss et al. 2015; Hutzler et al. 2014; Lisko et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Pyridine	110-86-1	100 µg/mL (Lim and Shin 2017)	(Aszyk, Kubica, et al. 2017; Lim and Shin 2017)
Raspberry ketone	5471-51-2	35 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Hutzler et al. 2014; Peace et al. 2017)
Sabinene	3387-41-5	1.5 µg/mL (Schober et al. 2014)	(Schober et al. 2014)
Sorbitol	50-70-4	-	(Miao et al. 2016)
Styrallyl acetate	93-92-5	13 µg/mL (Aszyk et al. 2018)	(Aszyk et al. 2018)
Styrallyl propionate	120-45-6	-	(Hutzler et al. 2014)
Syringol	91-10-1	-	(Hutzler et al. 2014)
Sucrose	57-50-1	620 µg/mL (Fagan et al. 2017)	(Fagan et al. 2017)
γ-Terpinen	99-85-4	-	(Hutzler et al. 2014)
α-Terpineol	98-55-5	350 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Sleiman et al. 2016)
α-Terpineol acetate	80-26-2	-	(Hutzler et al. 2014)
α-Terpinolene	586-62-9	-	(Hutzler et al. 2014)
δ-Tetradecalactone	2721-22-4	9.3 mg/mL (Bitzer, Goel, Reilly, Elias, et al. 2018)	(Bitzer, Goel, Reilly, Elias, et al. 2018)
Tetrahydrolinalool	78-69-3	120 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017; Aszyk et al. 2018)
2,3,5,6-Tetramethylpyrazine	1124-11-4	600 µg/mL (Tierney et al. 2016)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Tierney et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Theaspirane	36431-72-8	55 µg/mL (Aszyk, Wozniak, et al. 2017)	(Aszyk, Wozniak, et al. 2017)
3-Thujene	2867-05-2	-	(Hutzler et al. 2014)
Thujon	546-80-5	180 µg/mL (Hahn et al. 2014)	(Hahn et al. 2014)
p-Tolualdehyde	104-87-0	2.8 mg/mL (Tierney et al. 2016)	(Tierney et al. 2016)
Triethyl citrate	77-93-0	-	(Peace et al. 2017)
2,3,5-Trimethylpyrazine	14667-55-1	97 µg/mL (Lim and Shin 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Lim and Shin 2017; Schober et al. 2014)
γ-Undecalactone	104-67-6	500 µg/mL (Tierney et al. 2016)	(Eddingsaas et al. 2018; Aszyk et al. 2018; Hutzler et al. 2014; Peace et al. 2017; Tierney et al. 2016)
δ-Undecalactone	710-04-3	5.9 µg/mL (Schober et al. 2014)	(Schober et al. 2014)
γ-Valerolactone	108-29-2	88 µg/mL (Aszyk, Kubica, et al. 2017)	(Aszyk, Kubica, et al. 2017; Aszyk et al. 2018)
Vanillin	121-33-5	33 mg/mL (Tierney et al. 2016)	(Aszyk, Kubica, et al. 2017; Eddingsaas et al. 2018; Fagan et al. 2017; Aszyk et al. 2018; Hutzler et al. 2014; Schober et al. 2014; Sleiman et al. 2016; Tierney et al. 2016)
Veratraldehyde	120-14-9	360 µg/mL (Vardavas et al. 2017)	(Vardavas et al. 2017)

Chemical	CAS number	Maximum amount reported	Reference
Water	7732-18-5	26% (Geiss et al. 2015)	(Geiss et al. 2015)
3,4-Xylenol	95-65-8	40 µg/g (Varlet et al. 2015)	(Hutzler et al. 2014)

Appendix Table A3: Chemical contaminants in e-cigarette liquids

Chemical	CAS number	Maximum amount reported	Reference
Acetaldehyde	75-07-0	38 µg/mL (Hahn et al. 2014)	(Fagan et al. 2017; Farsalinos, Gillman, et al. 2015; Hahn et al. 2014; Sleiman et al. 2016; Varlet et al. 2015; LeBouf et al. 2018)
Acetamide	60-35-5	-	(Hutzler et al. 2014)
Acetone	67-64-1	20 µg/g (Varlet et al. 2015)	(Sleiman et al. 2016; Varlet et al. 2015; LeBouf et al. 2018)
Acetonitrile	75-05-8	-	(LeBouf et al. 2018)
Acrolein	107-02-8	10 ng/mL (Fagan et al. 2017)	(Fagan et al. 2017; Sleiman et al. 2016)
Aluminium	NA	15 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Olmedo et al. 2018)
Antimony	NA	1.5 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Olmedo et al. 2018)
Arsenic	NA	1.5 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Olmedo et al. 2018)
Benzene	71-43-2	2.3 µg /mL (Lim and Shin 2017)	(Lim and Shin 2017; LeBouf et al. 2018)
1,3-Butadiene	106-99-0	10 µg/mL (Varlet et al. 2015)	(Varlet et al. 2015)
Butanal	123-72-8	480 ng/mL (Varlet et al. 2015)	(Varlet et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Cadmium	NA	-	(Hess et al. 2017)
Catechol	120-80-9	1.7 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
4-Chloro-2,5-dimethoxyaniline	6358-64-1	-	(Hutzler et al. 2014)
Chlorpyrifos ethyl	2921-88-2	66 pg/mL (Beauval et al. 2017)	(Beauval et al. 2017)
Chromium	NA	7.7 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Hess et al. 2017; Olmedo et al. 2018)
Cobalt	NA	0.22 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017)
Copper	NA	-	(Olmedo et al. 2018)
m-Cresol	108-39-4	5.3 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
o-Cresol	95-48-7	5.5 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
p-Cresol	106-44-5	1.0 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
Crotonaldehyde	4170-30-3	84 ng/g (Varlet et al. 2015)	(Varlet et al. 2015)
Cyclohexane	110-82-7	11 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Dibutyl phthalate	84-74-2	400 ng/g (Moldoveanu and Yerabolu 2018)	(Moldoveanu and Yerabolu 2018)
Dichloromethane	75-09-2	-	(LeBouf et al. 2018)
Dicyclopentenyl alcohol	27137-33-3	-	(Hutzler et al. 2014)
Diethyl carbitol	112-36-7	-	(Hutzler et al. 2014)
Diethylene glycol	111-46-6	4 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Diethylhexyl phthalate	117-81-7	82 µg/mL (Oh and Shin 2015)	(Oh and Shin 2015; Moldoveanu and Yerabolu 2018)
Diethyl phthalate	84-66-2	1.8 mg/mL (Oh and Shin 2015)	(Eddingsaas et al. 2018; Moldoveanu and Yerabolu 2018; Oh and Shin 2015)
Diisobutyl phthalate	84-69-5	-	(Hutzler et al. 2014)
Dimethyl terephthalate	120-61-6	480 ng/g (Moldoveanu and Yerabolu 2018)	(Moldoveanu and Yerabolu 2018)
Ethoxytriglycol	112-50-5	-	(Hutzler et al. 2014)
Ethylbenzene	100-41-4	1.2 µg /mL (Lim and Shin 2017)	(Lim and Shin 2017; LeBouf et al. 2018)
Ethyl mandelate	774-40-3	-	(Hutzler et al. 2014)
Formaldehyde	50-00-0	28 µg/mL (Farsalinos, Gillman, et al. 2015)	(Fagan et al. 2017; Farsalinos, Gillman, et al. 2015; Sleiman et al. 2016; Varlet et al. 2015)
Glyceryl 1-monoacetate	106-61-6	-	(Eddingsaas et al. 2018; Hutzler et al. 2014)
Hexamethylenediol	629-11-8	-	(Hutzler et al. 2014)
Hexane	110-54-3	-	(LeBouf et al. 2018)
Homocamfin	28587-71-5	-	(Hutzler et al. 2014)
2-Hydroxyethyl salicylate	87-28-5	-	(Hutzler et al. 2014)
Iron	NA	-	(Olmedo et al. 2018)
Isopropyl alcohol	67-63-0	-	(LeBouf et al. 2018)
Isovaleric aldehyde	590-86-3	14 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Lead	NA	838 ng/mL (Dunbar et al. 2018)	(Dunbar et al. 2018; Hess et al. 2017; Olmedo et al. 2018)
Manganese	NA	3.3 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Hess et al. 2017; Olmedo et al. 2018)
Methanol	67-56-1	2.0 ng/mL (Lim and Shin 2017)	(Lim and Shin 2017)
2-Methyl-1,3-dioxane	626-68-6	57 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Methyl methacrylate	80-62-6	-	(LeBouf et al. 2018)
Methyltriglyme	112-49-2	-	(Hutzler et al. 2014)
Minor tobacco alkaloids	Multiple	740 µg/g (Lisko et al. 2015)	(Lisko et al. 2015; Hutzler et al. 2014)
Nickel	NA	-	(Hess et al. 2017; Olmedo et al. 2018)
Nitrate	14797-55-8	318 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
N-Nitrosonornicotine	16543-55-8	23 ng/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
2-Nitrothiophene	609-40-5	-	(Hutzler et al. 2014)
NNK	64091-91-4	22 ng/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)
Octamethyl-cyclotetrasiloxane	556-67-2	57 µg/mL (Lim and Shin 2017)	(Lim and Shin 2017)
4-tert-Octylphenol	140-66-9	-	(Hutzler et al. 2014)
p-Orcacetophenone	1634-34-0	-	(Hutzler et al. 2014)
Pentaethylene glycol	4792-15-8	25 µg/mL (Oh and Shin 2015)	(Oh and Shin 2015)
Phenol	108-95-2	3.7 µg/mL (Farsalinos, Gillman, et al. 2015)	(Farsalinos, Gillman, et al. 2015)

Chemical	CAS number	Maximum amount reported	Reference
Polycyclic Aromatic Hydrocarbons (PAH)	Multiple	66 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017; Geiss et al. 2015)
Propanal	123-38-6	260 ng/g (Varlet et al. 2015)	(Varlet et al. 2015)
1,2-Propanediol, 2-acetate	6214-01-3	-	(Eddingsaas et al. 2018)
1-Propanol	71-23-8	16 µg/g (Varlet et al. 2015)	(Varlet et al. 2015)
Propylene oxide	75-56-9	6.7 mg/mL (Sleiman et al. 2016)	(Sleiman et al. 2016)
Propyl isocyanate	110-78-1	-	(Hutzler et al. 2014)
Styrene	100-42-5	340 ng/mL (Lim and Shin 2017)	(Lim and Shin 2017; LeBouf et al. 2018)
Tetracosyl acetate	822-29-7	-	(Eddingsaas et al. 2018)
Tetraethylene glycol	112-60-7	30 µg/mL (Oh and Shin 2015)	(Oh and Shin 2015)
Tetraethylene glycol dimethyl ether	143-24-8	-	(Hutzler et al. 2014)
Tin	NA	-	(Olmedo et al. 2018)
Titanium	NA	-	(Olmedo et al. 2018)
Toluene	108-88-3	690 ng/mL (Lim and Shin 2017)	(Lim and Shin 2017; LeBouf et al. 2018)
Triethylene glycol	112-27-6	19 µg/mL (Oh and Shin 2015)	(Oh and Shin 2015)
Trifluralin	1582-09-8	25 pg/mL (Beauval et al. 2017)	(Beauval et al. 2017)
Tungsten	NA	-	(Olmedo et al. 2018)
Uranium	NA	-	(Olmedo et al. 2018)
Vanadium	NA	0.64 ng/mL (Beauval et al. 2017)	(Beauval et al. 2017)

Chemical	CAS number	Maximum amount reported	Reference
Xylene	1330-20-7	6.3 µg /mL (Lim and Shin 2017)	(Lim and Shin 2017; LeBouf et al. 2018)
Zinc	NA	38 µg/mL (Hahn et al. 2014)	(Olmedo et al. 2018)

Appendix Table A4: Chemical ingredients in e-cigarette emissions

Chemical	CAS number	Maximum amount reported	Reference
Acetoin	513-86-0	24 pg/mL emission (Klager et al. 2017)	(Allen et al. 2016; Klager et al. 2017)
Acetyl propionyl (2,3-Pentanedione)	600-14-6	1.1 pg/mL emission (Klager et al. 2017)	(Allen et al. 2016; Farsalinos, Kistler, et al. 2015; Klager et al. 2017)
2-Acetylpyrazine	22047-25-2	-	(Garcia-Gomez et al. 2016)
Allyl caproate	123-68-2	-	(Garcia-Gomez et al. 2016)
Benzaldehyde	100-52-7	180 µg/g e-cig liquid (Khlystov and Samburova 2016); 10 ng/mL emission (Klager et al. 2017)	(Khlystov and Samburova 2016; Klager et al. 2017; Kosmider et al. 2014; Kosmider et al. 2016; Sleiman et al. 2016)
Benzyl acetate	140-11-4	-	(Garcia-Gomez et al. 2016)
Butyl acetate	123-86-4	-	(Garcia-Gomez et al. 2016)
Butyl hexadecanoate	111-06-8	-	(Eddingsaas et al. 2018)
Butyl isovalerate	109-19-3	1.5 mg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Butyl octadecanoate	123-95-5	-	(Eddingsaas et al. 2018)

Chemical	CAS number	Maximum amount reported	Reference
Cadalene	483-78-3	-	(Eddingsaas et al. 2018)
Cadinol	11070-72-7	-	(Eddingsaas et al. 2018)
Carvone	99-49-0	-	(Garcia-Gomez et al. 2016)
1,8-Cineol	470-82-6	140 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Cinnamaldehyde	104-55-2	-	(Eddingsaas et al. 2018)
Citral	5392-40-5	-	(Garcia-Gomez et al. 2016)
Citronellol	106-22-9	-	(Eddingsaas et al. 2018)
Coumarin	91-64-5	-	(Garcia-Gomez et al. 2016)
Damascenone	23696-85-7	-	(Garcia-Gomez et al. 2016)
β-Damascone	23726-92-3	-	(Garcia-Gomez et al. 2016)
γ-Decalactone	706-14-9	-	(Eddingsaas et al. 2018)
δ-Decalactone	705-86-2	-	(Eddingsaas et al. 2018)
Decyl acetate	112-17-4	-	(Eddingsaas et al. 2018)
Diacetyl (2,3-Butanedione)	431-03-8	440 µg/g e-cig liquid (Sleiman et al. 2016); 3.7 pg/mL emission (Klager et al. 2017)	(Allen et al. 2016; Farsalinos, Kistler, et al. 2015; Klager et al. 2017; Margham et al. 2016; Garcia-Gomez et al. 2016; Sleiman et al. 2016)
3,4-Dihydrocoumarin	119-84-6	230 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
2,5-Dimethylpyrazine	123-32-0	-	(Garcia-Gomez et al. 2016)
1-Dodecanol	112-53-8	-	(Eddingsaas et al. 2018)
Ethanol	64-17-5	110 ng/mL emission (Lee et al. 2017)	(Lee et al. 2017)
Ethyl butyrate	105-54-4	1.6 mg/g e-cig liquid (Sleiman et al. 2016)	(Garcia-Gomez et al. 2016; Sleiman et al. 2016)
Ethyl caproate	123-66-0	-	(Garcia-Gomez et al. 2016)
Ethyl caprylate	106-32-1	-	(Garcia-Gomez et al. 2016)
Ethyl isovalerate	108-64-5	-	(Garcia-Gomez et al. 2016)
Ethyl maltol	4940-11-8	-	(Eddingsaas et al. 2018; Garcia-Gomez et al. 2016)
Ethyl α-methylbutyrate	7452-79-1	-	(Garcia-Gomez et al. 2016)
Ethyl salicylate	118-61-6	-	(Garcia-Gomez et al. 2016)
Ethyl vanillin	121-32-4	-	(Eddingsaas et al. 2018; Garcia-Gomez et al. 2016)
Eugenol	97-53-0	-	(Garcia-Gomez et al. 2016)
Glycerol	56-81-5	16 µg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Eddingsaas et al. 2018; Geiss et al. 2015; Jensen, Strongin, and Peyton 2017; Margham et al. 2016; Garcia-Gomez et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Hedione	24851-98-7	-	(Garcia-Gomez et al. 2016)
2,3-Heptanedione	96-04-8	0.53 pg/mL emission (Klager et al. 2017)	(Klager et al. 2017)
Hexadecanal	629-80-1	-	(Eddingsaas et al. 2018)
Hexaldehyde	66-25-1	4.5 mg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
2,3-Hexanedione	3848-24-6	3.2 pg/mL emission (Klager et al. 2017)	(Klager et al. 2017)
3,4-Hexanedione	4437-51-8	2.2 pg/mL emission (Klager et al. 2017)	(Klager et al. 2017)
1-Hexanol	111-27-3	-	(Eddingsaas et al. 2018)
Hexyl acetate	142-92-7	-	(Garcia-Gomez et al. 2016)
Hexyl hexanoate	6378-65-0	-	(Eddingsaas et al. 2018)
Hydroxyacetone	116-09-6	3.0 mg/g e-cig liquid (Sleiman et al. 2016)	(Jensen, Strongin, and Peyton 2017; Garcia-Gomez et al. 2016; Sleiman et al. 2016; Uchiyama et al. 2016)
Isoamyl isovalerate	659-70-1	-	(Garcia-Gomez et al. 2016)
Isobornyl acetate	125-12-2	-	(Garcia-Gomez et al. 2016)
Isomethyl-α-ionone	127-51-5	360 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Lauryl acetate	112-66-3	-	(Eddingsaas et al. 2018)
Limonene	138-86-3	660 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Linalol	78-70-6	-	(Garcia-Gomez et al. 2016)
Maltol	118-71-8	-	(Garcia-Gomez et al. 2016)
MDMB-FUBINACA	1715016-77-5	-	(Peace et al. 2017)
Menthol	1490-04-6	-	(Margham et al. 2016)
Menthone	89-80-5	-	(Garcia-Gomez et al. 2016)
1-(2-Methoxy-1-methylethoxy)-2-propanol	20324-32-7	-	(Eddingsaas et al. 2018)
2-Methylbutyrate	623-42-7	-	(Garcia-Gomez et al. 2016)
Methyl cinnamate	103-26-4	-	(Garcia-Gomez et al. 2016)
3-Methyl-1,2-cyclopentanedione	765-70-8	-	(Garcia-Gomez et al. 2016)
Methyl cyclopentenolone	80-71-7	-	(Garcia-Gomez et al. 2016)
2-Methylfuran	534-22-5	260 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Methyl heptanoate	106-73-0	-	(Eddingsaas et al. 2018)
Methyl hexadecanoate	112-39-0	-	(Eddingsaas et al. 2018)
Methyl hexanoate	106-70-7	-	(Eddingsaas et al. 2018; Garcia-Gomez et al. 2016)
Methyl octadecanoate	112-61-8	-	(Eddingsaas et al. 2018)
(E)-2-Methyl-2-pentenoic acid	16957-70-3	-	(Garcia-Gomez et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
2-Methylpyrazine	109-08-0	-	(Garcia-Gomez et al. 2016)
Methyl salicylate	119-36-8	-	(Garcia-Gomez et al. 2016)
Octadecanal	638-66-4	-	(Eddingsaas et al. 2018)
γ-Octalactone	104-50-7	-	(Garcia-Gomez et al. 2016)
Piperonal	120-57-0	-	(Eddingsaas et al. 2018)
Piperonal propylene glycol acetal	61683-99-6	-	(Eddingsaas et al. 2018)
Propylene glycol	57-55-6	23 µg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Eddingsaas et al. 2018; Geiss et al. 2015; Jensen, Strongin, and Peyton 2017; Margham et al. 2016; Garcia-Gomez et al. 2016)
α-Terpineol acetate	80-26-2	-	(Garcia-Gomez et al. 2016)
2,3,5,6-Tetramethylpyrazine	1124-11-4	-	(Garcia-Gomez et al. 2016)
p-Tolualdehyde	104-87-0	-	(Sleiman et al. 2016)
Tributyl acetylcitrate	77-90-7	-	(Eddingsaas et al. 2018)
2,3,5-Trimethylpyrazine	14667-55-1	-	(Garcia-Gomez et al. 2016)
γ-Undecalactone	104-67-6	-	(Eddingsaas et al. 2018)
Vanillin	121-33-5	200 µg/g e-cig liquid (Sleiman et al. 2016)	(Eddingsaas et al. 2018; Garcia-Gomez et al. 2016; Sleiman et al. 2016)

Appendix Table A5: Chemical reaction products in e-cigarette emissions during e-cigarette use

Chemical	CAS number	Maximum amount reported	Reference
Acetaldehyde	75-07-0	19.1 mg/g e-cig liquid (Sleiman et al. 2016); 48 ng/mL emission (Uchiyama et al. 2013)	(Beauval et al. 2017; Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Flora et al. 2017; Geiss et al. 2015; Goniewicz et al. 2014; Hutzler et al. 2014; Jensen, Strongin, and Peyton 2017; Klager et al. 2017; Khlystov and Samburova 2016; Kosmider et al. 2014; Laugesen 2015; Lee et al. 2017; Margham et al. 2016; Ogunwale et al. 2017; Sala et al. 2017; Sleiman et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016; Wang et al. 2017)
Acetic acid	64-19-7	-	(Jensen, Strongin, and Peyton 2017)
Acetone	67-64-1	1.4 mg/mL e-cig liquid (Sleiman et al. 2016); 5.3 ng/mL emission (Lee et al. 2017)	(Farsalinos, Voudris, and Poulas 2015; Geiss et al. 2015; Jensen, Strongin, and Peyton 2017; Kosmider et al. 2014; Lee et al. 2017; Margham et al. 2016; Ogunwale et al. 2017; Garcia-Gomez et al. 2016; Uchiyama et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Acrolein	107-02-8	10 mg/g e-cig liquid (Sleiman et al. 2016); 36 ng/mL emission (Uchiyama et al. 2013)	(Beauval et al. 2017; Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Flora et al. 2017; Geiss et al. 2015; Hutzler et al. 2014; Jensen, Strongin, and Peyton 2017; Khlystov and Samburova 2016; Laugesen 2015; Margham et al. 2016; Ogunwale et al. 2017; Sala et al. 2017; Sleiman et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016; Wang et al. 2017)
Allyl alcohol	107-18-6	820 µg/g e-cig liquid (Sleiman et al. 2016)	(Jensen, Strongin, and Peyton 2017; Margham et al. 2016; Sleiman et al. 2016)
Butanal	123-72-8	40 µg/g e-cig liquid (Sleiman et al. 2016)	(Kosmider et al. 2014; Margham et al. 2016; Ogunwale et al. 2017; Sleiman et al. 2016)
2-Butanone	78-93-3	1.9 mg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Crotonaldehyde	4170-30-3	720 µg/g e-cig liquid (Sleiman et al. 2016); 83 ng/mL emission (Klager et al. 2017)	(Flora et al. 2017; Klager et al. 2017; Kosmider et al. 2014; Sleiman et al. 2016)
Dihydroxyacetone	96-26-4	-	(Jensen, Strongin, and Peyton 2017)
1,2-Ethanediol, 1-(hydroxymethoxy)-	1823904-91-1	-	(Jensen, Strongin, and Peyton 2017)

Chemical	CAS number	Maximum amount reported	Reference
Ethanol, 1-(hydroxymethoxy)-	206360-28-3	-	(Jensen, Strongin, and Peyton 2017)
Formaldehyde	50-00-0	48 mg/g e-cig liquid (Sleiman et al. 2016); 99 ng/mL emission (Klager et al. 2017)	(Beauval et al. 2017; Farsalinos et al. 2018; Farsalinos and Voudris 2018; Farsalinos, Voudris, and Poulas 2015; Flora et al. 2017; Geiss et al. 2015; Goniewicz et al. 2014; Hutzler et al. 2014; Jensen et al. 2015; Khlystov and Samburova 2016; Klager et al. 2017; Kosmider et al. 2014; Laugesen 2015; Margham et al. 2016; Ogunwale et al. 2017; Sala et al. 2017; Salamanca et al. 2018; Sleiman et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016; Wang et al. 2017)
Formic acid	64-18-6	-	(Jensen, Strongin, and Peyton 2017)
Glyceraldehyde	56-82-6	-	(Jensen, Strongin, and Peyton 2017)
Glycidol	556-52-5	760 µg/g e-cig liquid (Sleiman et al. 2016)	(Jensen, Strongin, and Peyton 2017; Sleiman et al. 2016)
Glycolaldehyde	141-46-8	-	(Jensen, Strongin, and Peyton 2017)

Chemical	CAS number	Maximum amount reported	Reference
Glyoxal	107-22-2	150 µg/g e-cig liquid (Khlystov and Samburova 2016); 29 ng/mL emission (Uchiyama et al. 2013)	(Khlystov and Samburova 2016; Margham et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016)
Isobutyraldehyde	78-84-2	3.9 ng/mL emission (Klager et al. 2017)	(Klager et al. 2017)
Isovaleric aldehyde	590-86-3	-	(Kosmider et al. 2014)
Lactaldehyde	598-35-6	-	(Jensen, Strongin, and Peyton 2017)
Methacrolein	78-85-3	460 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
m-Methylbenzaldehyde	620-23-5	-	(Kosmider et al. 2014)
o-Methylbenzaldehyde	529-20-4	-	(Goniewicz et al. 2014; Kosmider et al. 2014)
Methylglyoxal	78-98-8	180 µg/g e-cig liquid (Sleiman et al. 2016); 22 ng/mL emission (Uchiyama et al. 2013)	(Margham et al. 2016; Sleiman et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016)
Propanal	123-38-6	3.2 mg/g e-cig liquid (Sleiman et al. 2016); 27 ng/mL emission (Uchiyama et al. 2013)	(Geiss et al. 2015; Hutzler et al. 2014; Jensen, Strongin, and Peyton 2017; Klager et al. 2017; Khlystov and Samburova 2016; Margham et al. 2016; Ogunwale et al. 2017; Sleiman et al. 2016; Uchiyama et al. 2013; Uchiyama et al. 2016)
1-Propen-1-ol	3965-44-4	-	(Jensen, Strongin, and Peyton 2017)

Chemical	CAS number	Maximum amount reported	Reference
Valeraldehyde	110-62-3	530 µg/g e-cig liquid (Sleiman et al. 2016); 6.6 ng/mL emission (Klager et al. 2017)	(Klager et al. 2017; Sleiman et al. 2016)

Appendix Table A6: Chemical contaminants in e-cigarette emissions

Chemical	CAS number	Maximum amount reported	Reference
Acetamide	60-35-5	-	(Garcia-Gomez et al. 2016)
Acetonitrile	75-05-8	0.9 ng/mL emission (Lee et al. 2017)	(Lee et al. 2017)
Arsenic	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Aluminium	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Antimony	NA	0.47 pg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Olmedo et al. 2018; Williams et al. 2017)
Barium	NA	-	(Lee et al. 2017; Williams et al. 2017)
Benzene	71-43-2	440 µg/g e-cig liquid (Sleiman et al. 2016); 6.6 ng/mL emission (Lee et al. 2017)	(Lee et al. 2017; Garcia-Gomez et al. 2016; Sleiman et al. 2016)
Boron	NA	-	(Williams et al. 2017)
Cadmium	NA	0.14 pg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Goniewicz et al. 2014; Olmedo et al. 2018)
Calcium	NA	-	(Williams et al. 2017)
Chlorine		-	(Lee et al. 2017)
Chromium	NA	3.4 pg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Margham et al. 2016; Olmedo et al. 2018; Williams et al. 2017)

Chemical	CAS number	Maximum amount reported	Reference
Cobalt	NA	-	(Williams et al. 2017)
Copper	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Diethyl phthalate	84-66-2	-	(Eddingsaas et al. 2018)
Dipropylene glycol	25265-71-8	-	(Garcia-Gomez et al. 2016)
3-Ethenylpyridine	1121-55-7	700 µg/g e-cig liquid (Sleiman et al. 2016)	(Sleiman et al. 2016)
Germanium	NA	-	(Williams et al. 2017)
Glycerol 1,2-diacetate	102-62-5	-	(Eddingsaas et al. 2018)
Glyceryl 1-monoacetate	106-61-6	-	(Eddingsaas et al. 2018)
Indium	NA	-	(Lee et al. 2017; Williams et al. 2017)
Iron	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Isopropyl alcohol	67-63-0	81 ng/mL emission (Lee et al. 2017)	(Lee et al. 2017)
Lanthanum	NA	-	(Williams et al. 2017)
Lead	NA	1.6 pg/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Goniewicz et al. 2014; Olmedo et al. 2018; Williams et al. 2017)
Magnesium	NA	-	(Williams et al. 2017)
Manganese	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Mercury	NA	-	(Williams et al. 2017)
Minor tobacco alkaloids	Multiple	7.0 mg/g e-cig liquid (Sleiman et al. 2016)	(Margham et al. 2016; Garcia-Gomez et al. 2016; Sleiman et al. 2016)

Chemical	CAS number	Maximum amount reported	Reference
Molybdenum	NA	-	(Williams et al. 2017)
1-Naphthalenol	90-15-3	-	(Eddingsaas et al. 2018)
NDMA	62-75-9	-	(Margham et al. 2016)
Nickel	NA	-	(Goniewicz et al. 2014; Margham et al. 2016; Olmedo et al. 2018; Williams et al. 2017)
N-Nitrosonornicotine	16543-55-8	-	(Goniewicz et al. 2014; Margham et al. 2016)
NNK	64091-91-4	-	(Goniewicz et al. 2014)
Octadecanamide	124-26-5	-	(Eddingsaas et al. 2018)
Polycyclic Aromatic Hydrocarbons (PAH)	Multiple	4.5 ng/mL emission (Beauval et al. 2017)	(Beauval et al. 2017; Margham et al. 2016)
Potassium	NA	-	(Williams et al. 2017)
1,2-Propanediol, 2-acetate	6214-01-3	-	(Eddingsaas et al. 2018)
Rubidium	NA	-	(Williams et al. 2017)
Selenium	NA	-	(Williams et al. 2017)
Silicon	NA	-	(Lee et al. 2017; Williams et al. 2017)
Silver	NA	-	(Williams et al. 2017)
Sodium	NA	-	(Williams et al. 2017)
Strontium	NA	-	(Williams et al. 2017)
Tin	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Titanium	NA	-	(Olmedo et al. 2018)

Chemical	CAS number	Maximum amount reported	Reference
Toluene	108-88-3	1.5 ng/mL emission (Lee et al. 2017)	(Goniewicz et al. 2014; Lee et al. 2017; Garcia-Gomez et al. 2016)
Tributyl aconitate	7568-58-3	-	(Eddingsaas et al. 2018)
Tungsten	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Vanadium	NA	-	(Williams et al. 2017)
Xylene	1330-20-7	-	(Goniewicz et al. 2014; Garcia-Gomez et al. 2016)
Zinc	NA	-	(Olmedo et al. 2018; Williams et al. 2017)
Zirconium	NA	-	(Williams et al. 2017)

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References highlighted in bold have disclosed assistance or a previous or current affiliation with industry associations or companies with an interest in e-cigarettes, tobacco, flavourings or tobacco cessation products.

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