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Delegations will find attached document COM(2016) 269 final.

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**REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND  
THE COUNCIL**

**on the potential risks to public health associated with the use of refillable electronic  
cigarettes**

## Background and context

Article 20(10) of Directive 2014/40/EU<sup>1</sup> ('Tobacco Products Directive' or 'TPD') requires the European Commission to submit a report to the European Parliament and the Council on the potential risks to public health associated with the use of refillable electronic cigarettes ('e-cigarettes'). At the time of the adoption of the TPD, there were concerns about the risks of refillable e-cigarettes to users and consumers, due to their particular characteristics, which allow users to come into direct contact with refill liquids ('e-liquids') containing nicotine and other ingredients which may have adverse health effects.

It should be noted that this report identifies the particular risks that may be associated with refillable e-cigarettes and their refill containers, as requested by the co-legislators. The report does not aim to make comparisons between refillable and other types of e-cigarettes, and does not consider the potential public health impact of e-cigarettes in general (such as initiation, cessation, dual use and long-term health effects).

E-cigarettes are relatively new products on the EU market and evidence concerning their potential risks and benefits is only starting to emerge. At this stage, the Commission and Member States are monitoring scientific evidence, user profiles and market developments regarding all types of e-cigarettes. This evidence will also inform the report on the application of the Tobacco Products Directive to be submitted from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions pursuant to Article 28 of the TPD.<sup>2</sup>

This report was prepared with input from the PRECISE study prepared by an external contractor.<sup>3</sup> This study analysed the available scientific literature on health risks of refillable e-cigarettes, data from EU poison centres in eight Member States, and performed chemical analysis on e-cigarette samples. The contractor also conducted a survey amongst the e-cigarette industry to determine what they believed to be the main risks associated with refillable e-cigarettes. The Commission has carefully considered the risks of refillable e-cigarettes identified by Member States and has discussed this report with the Expert Group on Tobacco Policy and the Subgroup on Electronic cigarettes.<sup>4</sup> Information based on discussions with international regulators has also been included in this report.

## Regulation of e-cigarettes under the Tobacco Products Directive

Article 20 of the TPD sets down a number of safety and quality requirements for nicotine-containing e-cigarettes intended for the consumer market. These consumer e-cigarettes may be disposable, rechargeable with a cartridge or refillable by means of refill containers containing e-liquid.

Manufacturers and importers must notify their products to Member State competent authorities (Article 20(2)). This notification must include information on ingredients and emissions, toxicological data, information on nicotine doses and uptake, and a description of the device and production

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<sup>1</sup> Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products and repealing Directive 2001/37/EC (OJ L 127, 29.04.2014, p. 1).

<sup>2</sup> Article 28(1) of the TPD requires that 'no later than five years from 20 May 2016, and whenever necessary thereafter, the Commission shall submit to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions a report on the application of this Directive.'

<sup>3</sup> EAHC/2013/Health/17: Potential Risks from Electronic Cigarettes and their Technical Specifications in Europe (PRECISE).

<sup>4</sup> Commission Decision of 4 June 2014 setting up the group of experts on tobacco policy, C(2014) 3509 final.

processes. Manufacturers must also submit sales data and information on consumer preferences annually to Member States (Article 20(7)). Manufacturers and importers must collect information on suspected adverse effects on human health and take immediate corrective action if they believe their products to be unsafe (Article 20(9)).

The TPD sets limits on the amount of nicotine in consumer e-cigarettes and refill containers. E-liquids must not contain more than 20 mg/ml nicotine (Article 20(3)(b)), tanks and cartridges must not be larger than 2 ml, and refill containers must not be larger than 10 ml (Article 20(3)(a)). Refill containers and e-cigarettes must also be child-resistant and tamper-proof, and sold with instructions for use and health warnings (Article 20 paragraphs 3(g), 4(a) and (b)).

### Potential risks to public health

The Commission has identified four main risks related to the use of refillable e-cigarettes. These risks are: (1) poisoning from ingesting e-liquids containing nicotine (especially for young children), (2) skin reactions related to dermal contact with e-liquids containing nicotine and other skin irritants, (3) risks associated with home blending and (4) risks due to using untested combinations of e-liquid and device or hardware customisation.

#### ***1. Accidental ingestion of e-liquid***

Refillable e-cigarettes and refill containers are, in most cases, open systems that allow direct access to nicotine-containing liquids. Nicotine is an alkaloid found in tobacco plants. It is a stimulant that acts on the parasympathetic nervous system and is the primary cause of addiction to tobacco products. A highly addictive drug, nicotine is also acutely toxic (lethal) by all routes of exposure in high enough doses.

In its opinion on the reclassification of nicotine, the European Chemical Agency's Committee for Risk Assessment (RAC) considered that 5 mg per kg bodyweight was a justified estimate for the acute toxicity of nicotine through oral exposure.<sup>5</sup> This Acute Toxicity Estimate (ATE) value is in the same order as outlined by Mayer (2014) who estimated the lower limit causing fatal outcomes as 0.5-1 g of ingested nicotine, corresponding to an oral LD50 of 6.5-13 mg per kg bodyweight for humans.<sup>67</sup> This translates to 390-780 mg of nicotine for a 60 kg adult and 65-130 mg for a 10 kg child.

Based on the limits set out in the TPD, refillable e-cigarette devices can contain up to 40 mg nicotine and refill containers can hold up to 200 mg nicotine. There is, therefore, a particular risk for young children if they accidentally ingest e-liquid especially from a refill container. There have been media reports of lethal poisonings of young children in the US and Israel from e-liquids.<sup>8</sup>

The PRECISE study commissioned for DG Health and Food Safety analysed 277 cases of nicotine poisoning reported to poison centres in eight EU Member States (Austria, Hungary, Ireland, Lithuania,

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<sup>5</sup> The European Chemicals Agency's Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of Nicotine (ISO). Adopted 10 September 2015. <http://echa.europa.eu/documents/10162/f9510930-4e5e-45ff-bb3a-888cefaf6592>.

<sup>6</sup> The LD50 value is a dose that, when administered to animals in an acute toxicity test, is expected to cause death in 50% of the treated animals in a given period.

<sup>7</sup> Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. Arch Toxicol 2014;88:5-7.

<sup>8</sup> <http://www.nydailynews.com/news/national/1-year-old-n-y-boy-dies-ingesting-liquid-nicotine-article-1.2045532> and <http://www.timesofisrael.com/police-investigating-toddler-death-from-nicotine-overdose/>.

Netherlands, Portugal, Sweden and Slovenia) from January 2012 to March 2015.<sup>9</sup> They found that 87.3% of cases were related to refill liquids, 0.7% to non-refillable e-cigarettes and 12% to unknown product types (which may partly be explained by their large market share). Of the cases studied, 71.3% related to unintentional poisoning. Overall, 67.5% of cases followed ingestion of e-liquids. In terms of demographics, 33.2% of cases related to children aged five or under, 9.7% related to 6-18 year olds and 57% related to adults over the age of 18. Regarding outcome, 23.7% of cases required hospitalisation and 6.8% had a moderate or major effect. These results are similar to data from US poison centres.<sup>10</sup>

Finally, it should also be noted that many different flavours are used in e-liquids; some of which are classified as hazardous to health under the CLP Regulation<sup>11</sup> and warrant further investigation.

### *How to mitigate risks?*

In order to mitigate the risk of accidental ingestion of nicotine-containing e-liquids, refill containers and e-cigarette devices should be child-resistant as laid down in Article 20(3)(g). Refillable e-cigarettes and their refill containers should also be sold with appropriate instructions for use and storage to prevent accidental ingestion of e-liquid by children or adults and warnings for specific risk groups (Article 20(4)(a)(i) and (iii)). They should also indicate a list of ingredients and be labelled with appropriate health warnings to communicate the potential health risks to consumers (TPD Article 20(4)(b) and the CLP Regulation). The rather high percentage of poisonings involving adults over the age of 18 (57%) also suggests the need to increase awareness amongst citizens on the toxicity of the e-liquids containing nicotine, perhaps through national educational campaigns.

In addition to these precautionary requirements, it is also important that other requirements are set for e-cigarettes; such as those laid down in Article 20(3) paragraphs (a) and (b) that ensure that e-liquid containers do not contain excessive levels of nicotine (which could be lethal to children and adults).

## **2. Dermal contact**

Refillable e-cigarettes require users to refill the device directly with e-liquid, usually using a small bottle or refill container. There is a risk when opening or refilling that e-liquid from refillable e-cigarettes is spilled and comes into contact with the skin. E-liquids contain substances that are toxic through dermal exposure (nicotine) or may be irritating to the skin (propylene glycol and flavours).<sup>12</sup>

In its Opinion on the reclassification of nicotine, the European Chemicals Agency's Committee for Risk Assessment<sup>13</sup> considered that 70 mg per kg bodyweight was a justified estimate for the acute toxicity of nicotine through dermal exposure.<sup>14</sup> This ATE value is identical to the LD50 derived from animal data, as the lethal dose of nicotine by the dermal route in humans is largely unknown. This would mean that at the concentrations allowed by the TPD, the amount of e-liquid needed to produce

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<sup>9</sup> EAHC/2013/Health/17: Potential Risks from Electronic Cigarettes and their Technical Specifications in Europe (PRECISE).

<sup>10</sup> Vakkalanka, J.P et al. Epidemiological trends in electronic cigarette exposures reported to U.S. Poison Centers. *Clinical Toxicology*, 2014;52(5): p. 542-548.

<sup>11</sup> Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353 31.12.2008, p. 1).

<sup>12</sup> Presentation by European Chemical Agency (ECHA) to the Subgroup on Electronic cigarettes on 14 March 2016.

<sup>13</sup> <http://echa.europa.eu/about-us/who-we-are/committee-for-risk-assessment>.

<sup>14</sup> The European Chemicals Agency's Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of Nicotine (ISO). Adopted 10 September 2015. <http://echa.europa.eu/documents/10162/f9510930-4e5e-45ff-bb3a-888cefaf6592>.

an acutely toxic effect through dermal exposure in humans is 35 ml for a small child and 210 ml for a 60kg adult. This is larger than the maximum size of a refill container allowed under the TPD. In their analysis of poison centre data, the PRECISE study also found that 10% of reported cases were related to dermal exposure.

Propylene glycol, a large component of many e-liquids, also appears to have mild irritating and sensitising effects on the skin of humans.<sup>15</sup> Some flavour components have also been self-reported as skin sensitizers or irritants in the European Chemicals Agency's C&L inventory.<sup>16</sup>

#### *How to mitigate risks?*

In order to mitigate the risk of dermal contact with nicotine-containing e-liquids, refill containers and e-cigarette devices should be child-resistant and protected against leakage (Article 20(3)(g)). They should also be refilled in a manner and be designed in a way that ensures refilling without leakage as laid down in Article 20(3)(g), and specified further by Commission Implementing Decision (EU) 2016/586.<sup>17</sup> Refillable e-cigarettes and their refill containers should also be sold with appropriate instructions for use and storage to ensure that users and others do not accidentally come into contact with the e-liquid when handling e-cigarettes and information on possible adverse effects (Article 20(4)(a)(i) and (iv)). E-cigarettes should also be labelled according to the requirements set out in the TPD (Article 20(4)(b)) and those specified under other relevant EU legislation (such as the CLP Regulation).

### **3. *Mixing or customisation of liquids***

Unlike disposable or rechargeable e-cigarettes, refillable e-cigarettes allow users more flexibility to determine the e-liquid used in their devices. Although the majority of users purchase e-liquids pre-blended, some users prefer to blend their own e-liquid at home by purchasing ingredients separately (home blending or self-mixing).<sup>18</sup> Refillable e-cigarettes may also allow users to 'customise' their e-liquid according to personal preferences by, for example, mixing flavours. There are a number of risks associated with these practices.

Firstly, home blending requires that users purchase high-concentration nicotine. E-liquid is, for example, sold in 50 ml bottles containing 72 mg/ml nicotine (3.6g of nicotine per bottle).<sup>19</sup> As outlined previously, there are risks to users and others if high concentrations of nicotine liquid are stored at home and handled inappropriately. There is also a risk that consumers do not dilute the solution correctly resulting in much higher nicotine concentrations than intended in the final e-liquids. Although the TPD introduces maximum nicotine concentration levels for e-cigarettes (e-liquids must not contain more than 20 mg/ml nicotine) and limits the volume of refill containers (they must not be larger than 10 ml), there is a risk that home blending may also allow users to circumvent the limits set for e-cigarettes in the TPD (through the purchase of high concentration nicotine or nicotine in powdered form if not adequately controlled by Member States).

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<sup>15</sup> Health Council of the Netherlands. Propylene glycol (1,2-Propanediol); Health based recommended occupational exposure limit. The Hague: Health Council of the Netherlands, 2007; publication no. 2007/02OSH.

<sup>16</sup> <http://echa.europa.eu/eu/information-on-chemicals/cl-inventory-database>.

<sup>17</sup> Commission Implementing Decision (EU) 2016/586 of 14 April 2016 on technical standards for the refill mechanism of electronic cigarettes (OJ L 101, 16.4.2016, p. 15)

<sup>18</sup> According to the Industry Organisation ECITA, home blending is limited to less than 5% of the market, [http://ec.europa.eu/health/tobacco/docs/ev\\_20131122\\_mi\\_en.pdf](http://ec.europa.eu/health/tobacco/docs/ev_20131122_mi_en.pdf).

<sup>19</sup> <https://www.totallywicked-liquid.com/50-ml-titanium-ice-72-mg-unflavoured-3-bottle-multipack.html>.

The TPD requires manufacturers or importers to submit data on toxicological studies (Article 20(2)(c)) and to ensure that only high-purity ingredients are used in e-liquids (Article 20(3)(d)). Home blending would mean that untested e-liquids with inappropriate ingredients could continue to be used by consumers.

Secondly, many of the flavours currently in use in e-liquids have not been tested for use in e-liquids and it is not known if they are safe for inhalation. There is evidence emerging that some flavours are not safe when used in e-cigarettes.<sup>20</sup> One concern is that refillable e-cigarettes will allow users to continue to use untested or unsafe flavours. Users could also potentially mix flavours with unknown effects (either through home-blending or adding additional flavours to purchased e-liquids ('customising')). The health risks of second-hand exposure of vapour from such self-mixed e-liquids are also unknown.<sup>21</sup>

An additional concern is that refillable e-cigarettes may be used with illegal substances such as tetrahydrocannabinol (THC). In a study of 3,847 students in the United States, 5.4% had used e-cigarettes to vaporise cannabis. Of those that had ever used e-cigarettes, 18% had used them to vaporise cannabis.<sup>22</sup>

#### *How to mitigate risks?*

In order to mitigate the risks associated with home blending or e-liquid customisation, Member States should ensure that manufacturers and importers respect the limits on nicotine concentration set by the TPD. The TPD does not allow e-liquids of concentrations higher than 20 mg/ml or in containers larger than 10 ml. Similarly, high-concentration liquid or powdered nicotine for other purposes, such as industrial use, should not be easily accessible for consumer purchase. If they do not already do so, Member States should also consider regulating or limiting the sale of such solutions or powders. Authorities should also ensure that oils or liquids with THC or other illicit substances are not sold to consumers in Member States where they are not allowed.

Member States should also monitor notifications and conduct research on the toxicological profile of e-liquids and emissions as regards flavours and the mixing of flavours in notified products. Member States should carefully monitor evidence on the health risks of flavours. As additional evidence emerges, it may be justified for Member States to prohibit certain flavours for use in e-liquids (as outlined in Recital 47 of the TPD, the responsibility for adopting rules on flavours remains with the Member States).

#### ***4. Use of e-liquids with untested devices and hardware customisation***

Refillable e-cigarettes allow users to mix and match e-liquid and devices and to customise their devices by purchasing components separately and 'building' their own device (also known as hardware customisation).<sup>23</sup>

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<sup>20</sup> Barrington-Trimis, J.L et al..Flavorings in electronic cigarettes: an unrecognised respiratory health hazard? *Jama*, 2014. 312(23): p. 2493-4.

<sup>21</sup> US CDC Letter of Evidence on e-cigarettes to N.C. Department of Health and Human Services. <http://www.tobaccopreventionandcontrol.ncdhhs.gov/Documents/CDC-LetterofEvidenceonElectronicNicotineDeliverySystemsNorthCarolina-April2015.pdf> .

<sup>22</sup> Morean et al. High School Students' Use of Electronic Cigarettes to Vaporize Cannabis. *Pediatrics* 2015;136:4.

<sup>23</sup> Individual e-cigarette components can easily be purchased and configured together to make customised devices (e.g. <http://www.amazon.co.uk/ecigarette-eshisha/b?ie=UTF8&node=3787506031>).

Studies have also shown that if e-liquid is heated to higher temperatures, an increase in toxic emissions is observed.<sup>24</sup>

There is a risk therefore that the combination of device and e-liquid chosen by users will not have been adequately tested, in particular as regards the safety of the emissions produced. Hardware customisation may further mean that users boost e-cigarettes with powerful batteries, increasing the amount of toxic emissions, although it should be noted that vapour heated to a very high temperature may not be palatable to users.

There is also a risk to users if untested or inappropriate components are used, such as leaching of metals into the e-liquid or battery explosions.<sup>25</sup> According to Article 20(2)(e) to (g) of the TPD, manufacturers and importers must include a description of the components used, the production process and a declaration that they bear full responsibility for the safety and quality of the products they place on the market.

#### *How to mitigate risks?*

Member States should ensure when enforcing the TPD that manufacturers and importers of e-cigarettes do not sell untested components and that all notified components have undergone appropriate tests to ensure they are safe. Member States should also ensure that when manufacturers and importers notify information on e-liquids they consider the conditions under which they can reasonably be expected to be used by consumers.

Member States should also ensure that notifications received under the TPD accurately reflect whether particular components or devices have the potential to significantly affect the quality of the emissions produced or increase their toxicity depending on the way in which they are used. Member States should also ensure that when measures are taken on dangerous products posing a risk to the health and safety of consumers they are notified through the Rapid Alert System for dangerous non-food products ('RAPEX')<sup>26</sup>, allowing other countries that may find the same product in their national markets to take the necessary measures to prevent the further sale of the dangerous product.

#### Conclusions

The use of refillable electronic e-cigarettes, and the potential exposure to e-liquids containing nicotine in high concentrations, may pose risks to public health. In the context of current scientific knowledge, the measures relating to refillable e-cigarettes provided for in the TPD and secondary legislation,<sup>27</sup> combined with national regulation, provide an adequate and proportionate framework for the mitigation of such risks. This does not, however, preclude the need for further study of these products and their safety for consumers (in particular concerning poisoning from accidental ingestion of e-liquid and the hazard profile of flavours). There is also a need for raised awareness amongst citizens of the toxicity of the e-liquids containing nicotine, which could potentially be achieved through national educational campaigns.

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<sup>24</sup> Geiss, O., et al., Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *Int. J. Hyg. Environ. Health.* 2016. 219(3): p.268-277, <http://dx.doi.org/10.1016/j.ijheh.2016.01.004>.

<sup>25</sup> Brown CJ, et al. Electronic cigarettes: product characterization and design considerations. *Tob Control* 2014;23:ii4–ii10. doi:10.1136/tobaccocontrol-2013-051476.

<sup>26</sup> [http://ec.europa.eu/consumers/consumers\\_safety/safety\\_products/rapex/index\\_en.htm](http://ec.europa.eu/consumers/consumers_safety/safety_products/rapex/index_en.htm).

<sup>27</sup> Commission Implementing Decision (EU) 2016/586 of 14 April 2016 on technical standards for the refill mechanism of electronic cigarettes (OJ L 101, 16.4.2016, p. 15)

Member States and the Commission should carefully monitor the market of refillable e-cigarettes, as well as the notifications received under Article 20(2) of the TPD. Further research on certain aspects of e-cigarettes relevant to refillables, such as emissions testing and the safety of flavours or mixtures of flavours, should also be carried out. Additional research on these topics would benefit all users of e-cigarettes (disposable, rechargeable and refillable).