About Public Health England and the Medicines and Healthcare products Regulatory Agency

Public Health England exists to protect and improve the nation’s health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health, and a distinct delivery organisation with operational autonomy to advise and support government, local authorities and the NHS in a professionally independent manner.

The Medicines and Healthcare products Regulatory Agency regulates medicines, medical devices and blood components for transfusion in the UK. Medicines and Healthcare products Regulatory Agency is an executive agency, sponsored by the Department of Health.

1. Introduction

1.1 Public Health England (PHE) is the government agency with responsibility for protecting and improving the nation’s health and wellbeing and reducing health inequalities. PHE advises government on the evidence on e-cigarettes (e-cigs). The Medicines and Healthcare products Regulatory Agency (MHRA) regulates medicines, medical devices and blood components for transfusion in the United Kingdom (UK) and is the competent authority for the UK notification scheme for e-cigs and nicotine-containing refill containers (e-liquids).

1.2 The UK is a leader in tobacco control and ranks top in the scale of tobacco control activity in 35 European nations. Smoking rates in the UK have fallen to their lowest recorded levels among both adults and youth. However, smoking remains the leading cause of premature death and the single largest driver of health inequalities.

1.3 E-cigs have rapidly become the most popular stop smoking aid in England. Evidence is evolving and early studies indicate that they are effective in smoking cessation (comparable to licensed nicotine replacement medicines).

1.4 As relatively new products, long-term evidence on e-cigs does not yet exist. They are unlikely to be risk free. However, there is good reason to believe that they are substantially less harmful than smoking tobacco, estimated to be around 95% less harmful in PHE’s independent review conducted in 2015, and by the Royal College of Physicians in 2016.
Written evidence submitted by Public Health England and the Medicines and Healthcare products Regulatory Agency (ECG0081)

1.5 British youth experiment with e-cigs but regular use is rare and very largely confined to young people who have smoked. There is some evidence that young people who have vaped but never smoked are more likely subsequently to smoke but there is no evidence that this relationship is causal. The UK has good data on this issue from surveys and we continue to scrutinise these data closely.

1.6 The number of poisonings in England involving e-cigs is low and severe poisonings are very rare. Numbers of reported poisonings fell somewhat coinciding with the introduction of new safety regulations in May 2016.

1.7 The UK has a new and comprehensive array of regulations for e-cigs. The recent Tobacco Control Plan for England commits the government to reviewing these regulations.

2. The impact on human health

2.1 There has been no opportunity yet to assess long-term benefit or harms of direct e-cigs use or of indirect exposure to e-cigs aerosol. In the meantime, public health advice has depended upon quantitative chemical and toxicological approaches to model the comparative risks associated with e-cigs compared with tobacco cigarettes. In addition there are limited clinical and short-term epidemiological studies comparing the safety of e-cigs with smoking tobacco.

Cancer

2.2 Levels of carcinogenic chemicals (including polycyclic aromatic hydrocarbons, tobacco-specific N-nitrosamines, heavy metals and volatile organic compounds are substantially lower in e-cigs’ aerosol compared with tobacco smoke. Biomarkers of carcinogen exposures (chemicals detected in the blood or urine of users) are also substantially decreased in current e-cig only users compared with cigarette smokers and decrease when smokers switch to e-cigs.

2.3 A recent cancer risk model based on published levels of 15 carcinogens in tobacco smoke and in e-cig aerosol and the lifetime cancer risk associated with these exposures suggests that the mean lifetime cancer risk for e-cig products would be 0.004 times that for smoking tobacco (less than 1%). Certain e-cig settings generate larger concentrations of carbonyls (including formaldehyde) and these would be expected to be associated with a higher cancer risk. Data were excluded from the model estimate above where these settings were used because they tend to produce a vapour that is aversive to users.

2.4 It is too early to observe directly how these reductions in carcinogen exposure translate into lower cancer incidence.
Respiratory and cardiovascular disease

2.5 There has been less research published on other health consequences of smoking such as chronic obstructive pulmonary disease and cardiovascular disease (CVD). However, as for cancer one could reasonably assume that risks would be much reduced because the chemicals linked with these risks are either absent or present at much lower levels in e-cig vapour.

2.6 With respect to clinical studies, a three and a half year longitudinal study in a small cohort of e-cig users who were never smokers has demonstrated no significant detrimental effects on lung function, heart rate or blood pressure compared with a control population. Data on the effects of e-cig on CVD are limited. Short-term effects are mostly commensurate with the known effects of nicotine such as transiently increased heart rate and increased blood pressure while acute endothelial cell dysfunction and oxidative damage have also been shown. The consequences of these transient effects on CVD risk are currently unclear.

2.7 A reduction in carboxyhaemoglobin, a biomarker of carbon monoxide exposure, to levels found in non-smokers is observed in e-cig users. This is highly beneficial as it increases oxygen carrying capacity of the blood, which means that the heart has to work less hard.

Second-hand exposure

2.8 Second-hand exposure to potential toxicants in e-cig aerosol is substantially lower than that from second-hand tobacco smoke. E-cigs aerosol contains substantially lower toxicant concentrations and is much less dispersed in the environment than tobacco smoke. One reason for lower dispersal is that second-hand e-cig exposure is only from mainstream expired breath as there is no side-stream exposure.

2.9 Particulate exposure is also significantly reduced in second-hand e-cigs aerosol compared with second-hand tobacco smoke. Data on second-hand nicotine exposure vary between studies from comparable to smoking to very much lower.

2.10 The health risks associated with second-hand e-cig aerosol exposure are therefore likely to be substantially lower than those from second-hand tobacco exposures.

Public perceptions of harm

2.11 Public perceptions of the harmfulness of e-cigs have become increasingly inaccurate over recent years. Between 2013 and 2017 the proportion of smokers in Britain who think e-cigs are at least as harmful as smoking increased from 9% to 22%, a belief that is correlated to a reduced likelihood to try e-cigarettes and a
3. The benefits and risks as a ‘stop smoking’ tool

3.1 E-cigs are the most popular stop smoking aid in England.\textsuperscript{xxv} There is evidence that they can help smokers to quit or, for those who are not ready to stop in one step, to reduce their cigarette consumption.\textsuperscript{xxvi}

3.2 Two randomised controlled trials have shown that e-cigs with nicotine help smokers stop smoking compared with placebo (no nicotine e-cigs).\textsuperscript{xxvii, xxviii} The effect size was similar to that found with licensed nicotine products when prescribed by a health professional.

3.3 National monitoring data show that smokers who combine e-cigarette use with support from their local stop smoking service have the highest quit rates, with two thirds quitting successfully compared with half of those using licensed nicotine replacement therapy products. However the proportion of clients using e-cigs in a quit attempt is only 4% of the total.\textsuperscript{xxix}

3.4 It is estimated that e-cigs contribute an additional 16,000 - 22,000 ex-smokers nationally per year beyond those who would be expected to quit through other means.\textsuperscript{xxx}

3.5 Many e-cigs users report that these devices help them to either quit or cut down smoking.\textsuperscript{xxxi, xxxii, xxxiii, xxxiv, xxv} Among a group of smokers who were using e-cigs and smoking, 46% had stopped smoking one-year later.\textsuperscript{xxxi} In another study, smokers were more likely to quit using e-cigs than with nicotine replacement therapy (NRT) purchased over the counter, but quit rates were similar to licensed medicines obtained on prescription.\textsuperscript{xxxvii}

3.6 A United States study found intensive use was associated with a greater chance of quitting smoking.\textsuperscript{xxxviii} Others have reported that smokers who use e-cigs may be less likely to quit than non-e-cigs users. However, these data are difficult to interpret because of limitations such as the definition of e-cig use (e.g. ever use vs. daily use) and not controlling for potential confounding factors (smoking history and environmental factors).
Dual use

3.7 The issue of ‘dual use’ and its impact on the likelihood of subsequent smoking cessation is one of the more hotly contested areas of the academic debate on e-cigs. As with licensed NRT, a significant proportion of e-cigs users currently smoke.

3.8 The evidence on the impact of dual use from international studies is mixed, with outcomes being affected by the type of device and frequency of use. Caponnetto found that when smokers who had refused help to quit were provided with e-cigs around 10% were abstinent from tobacco at 12 months. This is comparable to smokers making a quit attempt with NRT. A systematic review of NRT use among smokers not intending to quit had similar conclusions.

3.9 In Britain, 1.5 million vapers have managed to stop smoking completely and a further 770,000 have given up both smoking and vaping, suggesting that for many smokers, dual use is a stage in their journey to becoming tobacco free and, ultimately, nicotine free.

4. Uptake among young people and evidence on whether e-cigarettes play a role in ‘re-normalising’ smoking

4.1 There are two major concerns about e-cigs use among young people, firstly that they may provide a ‘gateway’ into smoking and secondly that they may ‘renormalise’ smoking. Neither term is well defined in a way that makes them open to objective testing.

4.2 ‘Denormalising’ and ‘renormalising’ smoking are particularly poorly defined in this context. By conspicuously replacing smoking, e-cigs may indeed reinforce social norms against smoking. We are not aware of any studies that offer conclusive findings.

4.3 The ‘gateway hypothesis’ may be described as the notion that the use of one substance leads causally to the regular use of a second.

4.4 Several studies, including from the UK, have suggested that young people who have never smoked are more likely to smoke subsequent to experimentation with e-cigs. These studies generally start by excluding all youth who have smoked and look for young people who have not smoked yet but have used e-cigs at least once. They find that these young people are more likely to try smoking at
4.5 These studies demonstrate that some young people try e-cigs before they try smoking. They do not demonstrate that their e-cig use causes them to try smoking. Nor do they strongly demonstrate that they become established smokers. There are many factors which influence young people to smoke and these seem likely to be similar to those that lead people to try e-cigs.

4.6 If e-cigs were acting substantially as a ‘gateway’ to tobacco use one might expect to see an increase in youth smoking with the rise in popularity of e-cigs. The Smoking, Drinking and Drug Use among Young People in England survey demonstrates a large decline in 15 year old regular (weekly) smokers (figure 1).

Figure 1: Trend in 15 year old regular smokers (SDD)

4.7 The SDD showed an increase in young people (age 11-15 years) using e-cigs between 2014 and 2016 (table 1) but regular use is almost entirely in smokers and ex-smokers (figure 2).
Table 1: E-cigarette status of young people (age 11-15 years) by sex and survey year (SDD)

<table>
<thead>
<tr>
<th>E-cigarette status</th>
<th>Males</th>
<th></th>
<th></th>
<th>Females</th>
<th></th>
<th></th>
<th>Persons</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Current e-cigarette user</td>
<td>4.5</td>
<td>7.3</td>
<td>3.5</td>
<td>5.0</td>
<td>4.0</td>
<td>6.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever used e-cigarettes</td>
<td>23.3</td>
<td>27.4</td>
<td>20.5</td>
<td>23.0</td>
<td>21.9</td>
<td>25.2</td>
<td></td>
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</tr>
</tbody>
</table>

4.8 A large study of e-cigs use among young people in the UK found that although experimentation with e-cigs was not uncommon among young people, regular use was rare and very largely confined to young people who had already smoked.xlv

Figure 2: Regular e-cigarette users, age 11-15 years, by smoking status (SDD)

4.9 In line with other studies, the SDD survey finds younger respondents were least likely to have ever used an e-cig, with 8% of 11 year olds ever having tried an e-cigarette and just 1% of those being current users compared with 41% of 15 year olds having ever tried an e-cigarette and 11% of those being current e-cig users (figure 3).
5. Regulatory variation between the EU and the UK

5.1 The UK has one of the most comprehensive regulatory systems for e-cigs in the world including long standing restrictions on advertising and marketing, minimum standards of quality and safety under the Tobacco and Related Products Regulations 2016 (TRPR) and a minimum age of sale of 18.

5.2 The bulk of e-cigarette regulation in Europe is based on the EU Tobacco Products Directive (2014/40/EU). This is transposed into UK law by the Tobacco and Related Products Regulations 2016 (TRPR).

5.3 The MHRA is the UK competent authority for the notification of e-cigs and nicotine-containing refill containers. Full details of the operation of the scheme have been published.

5.4 Anyone who manufactures or imports these products or who re-brands any product must submit information about their products to MHRA. MHRA has published comprehensive guidance on the notification requirements.

5.5 A submission must be made six months before the intended launch of the product. MHRA has worked with the industry to ensure that unnecessary delays are not encountered in launching new products. The process is designed to ensure that products can be added on the published notification list within one month of the date of submission. Once the product is listed, the company is free to start selling it in the UK, without further delay.
5.6 Over 32,000 product notifications have been received and published by the MHRA since the start of the scheme. About 90% are e-liquids and the remainder, devices and kits.

5.7 The notification scheme relies on declarations made by the producer that their product complies with the legal requirements and that the notifier takes full responsibility for the quality and safety of the product.

5.8 There is no requirement to notify refill containers that do not contain nicotine when sold. These products continue to be regulated under the General Product Safety Regulations.

5.9 The MHRA also provides an option for medicinal regulation of e-cigs. MHRA has published specific guidance on the procedure to licence e-cigs and other nicotine-containing products as medicines. Scientific advice meetings have also been held with a number of companies to facilitate applications. To date, MHRA has authorised one e-cig product as a medicine.

6. Brexit

6.1 The Tobacco Control Plan for England states: “Over the course of this Tobacco Control Plan, the government will review where the UK’s exit from the EU offers us opportunities to re-appraise current regulation”. PHE has been commissioned to repeat its evidence updates annually for the duration of this Parliament, providing evidence to inform Government policy.

7. Regulation on advertising and marketing

7.1 In 2017 the UK Committee of Advertising Practice and Broadcast Committee of Advertising Practice conducted a public consultation on changes to their Codes to remove the current prohibition on health claims being made for non-medicinal e-cigs.

7.2 Based on the existence of comprehensive regulation and evidence that despite the substantially reduced risk, smokers increasingly believe e-cigs are as harmful as smoking, PHE supported the proposals.

7.3 In relation to public health advertising, PHE recommended that any organisation with a vested commercial interest may promote public health messages in relation to e-cigs as a product category only through support of a campaign from an independent and reputable health body.
8. Impact of the regulations on the vaping industry and on prevalence of use

8.1 The TRPR came fully into force in May 2017. The most up to date published data is from the Action on Smoking and Health Smokefree GB data and the fieldwork for this was completed in the spring of 2017. Consequently there is no available survey data that can demonstrate the impact of TRPR on consumption. However, we are able to offer new analysis of official data that the Committee may find of use.

8.2 The Office for National Statistics (ONS) Annual Population Survey shows that the trend in prevalence of current smokers has been decreasing in recent years, from 19.3% of adults (age 18+ years) in 2012 to 15.5% in 2016.

8.3 There was a clear gradient by deprivation, with 18.8% of the most deprived decile being current smokers, compared with 11.8% of the least deprived.

8.4 In 2016, 18.4% of adults (age 16+ years) surveyed in the ONS Opinions and Lifestyle Survey had tried an e-cigarette and 5.4% of adults considered themselves current e-cigarette users. This continues the increasing trend seen in recent years (figure 4).
8.5 Use of e-cigs is almost entirely by current and ex-smokers, and less than 1% of adults who had never smoked were current vapers (figure 5).
9. The safety of e-cigarette devices and any safety regulation requirements

9.1 MHRA monitors the safety of products through the Yellow Card reporting system allowing consumers and healthcare professionals to report side effects and safety concerns with e-cigs or refill containers.

9.2 Only a small number of Yellow Card reports of adverse effects have been received and no evidence of new risks has been identified as a result of the data collected so far.

9.3 Reports of quality concerns or device defects received by MHRA are sent to the producer for further investigation or to local Trading Standards teams for action as necessary.

9.4 The PHE-commissioned National Poisons Information Service (NPIS) provides advice to UK healthcare professionals on poisonings through an online database TOXBASE and a 24-hour telephone service.

9.5 The number of TOXBASE enquiries relating to e-cigs increased more than 10 fold from January 2013 (28) to its peak in January 2016 (394). Since then the number of enquiries has declined and touched a three year low in December 2016. This decline may be a result of the implementation of the TRPR from May 2016, although it appears to have started prior to their introduction.

9.6 A similar pattern is observed in enquiries to NPIS, which peaked in 2015/6 (272 cases). There was a decline in accidental poisonings in 2016/7 (185) compared to 2015/6 (228) or 2014/5 (206). Over the past for four years, the average poisoning severity associated with e-cigs has ranged from “none” or “minor” for over 95% of exposures (902 cases) with >2% rated as moderate (20 cases) and <1% rated as severe (7 cases). Relatively few of the exposures result in severe features, but it is of note that all five of the cases with severe features in the last two years were associated with cardiac arrest.

9.7 Enquiries on cases involving e-cigs account for a tiny proportion of the total received by NPIS: 0.4% in 2013-14, 0.52% in 2014-15, 0.58% in 2015-16 and 0.53% in 2016-17.
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Figure 6: Monthly TOXBASE enquiries

![Monthly TOXBASE enquiries relating to e-cigarettes (Jan 2010 - Oct 2017)](image)

Figure 7: NPIS reports of poisoning

![NPIS e-cigarette poisoning reports and severity (2013-17)](image)
10. Public finances implications of e-cigarettes

10.1 There are currently insufficient data to make a reliable assessment on the near-term impact of e-cigs on healthcare costs. Any estimates should be treated with caution.

10.2 The evidence on the reduction of cancer risk is strong but the impact is likely only to be accrued in the long term. The evidence of reduction of risk for respiratory and cardiovascular disease, although encouraging, is less clear.

10.3 Any model would need to consider the demographics of e-cig use. Switching among smokers who are already being treated for smoking-related illness is likely to have a greater short-term impact on care costs. Switching among healthy and younger smokers is likely to deliver savings only in the longer term.

11. Novel tobacco products including ‘heat not burn’ products

11.1 Novel tobacco products are regulated under the TRPR and PHE is designated as the competent authority. Only two brands of product have been notified as novel tobacco products.

11.2 In 2017 the scientific advisory committees on Toxicity, Carcinogenicity and Mutagenicity conducted an inquiry into ‘heat not burn’ tobacco products and the report is expected to be published shortly. PHE’s next independent review of the evidence on e-cigs, to be published early in 2018, will include an analysis of the available independent data on ‘heat not burn’ products.

12. Concluding comments

12.1 In summary, e-cigs will improve public health if they become a route out of smoking for large numbers of adult smokers, without providing a route into smoking for children and non-smokers or generating new health risks. It is our view that the evidence to date suggests that this is the case. Close monitoring of uptake, safety and effectiveness and appropriate and proportionate regulation remain essential safeguards.

December 2017
13. References

i In this submission we use the term e-cigarettes (ECs) to refer to products that heat a nicotine containing liquid as distinct from products that heat tobacco.


iii “Nicotine without smoke: tobacco harm reduction”, Royal College of Physicians, April 2016 https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0


vii Etter and Bullen 2017 A longitudinal study of electronic cigarette users. Addictive Behaviours 39, 491-494

viii Polosa et al 2017 Health impact of E-cigarettes: a prospective 3.5-year study of regular daily users who have never smoked. Scientific Reports 7, 13825

ix Stephens 2017 Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. Tob Control 0, 1-8.


xviii Goniewicz et al (2017) Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. Tob Control 2014;23: 133–139

xix Schick SF, Glantz SA. Phillip morris toxicological experiments with fresh sidestream smoke: more toxic than mainstream smoke. Tob Control 2005;14:396–404

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xiv ASH (May 2017) Use of e-cigarettes (vapourisers) among adults in Great Britain

xxv Smoking Toolkit Study, http://www.smokinginengland.info/


xxix Statistics on NHS Stop Smoking Services: England, April 2016 to December 2016, NHS Digital, April 2017


x Moore David, Aveyard Paul, Connock Martin, Wang Dechao, Fry-Smith Anne, Barton Pelham et al. Effectiveness and safety of nicotine replacement therapy assisted reduction
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to stop smoking: systematic review and meta-analysis BMJ 2009; 338 :b1024


Soneji, Samir, James D. Sargent, Susanne E. Tanski, and Brian A. Primack. 


ASH (May 2017) Use of e-cigarettes (vapourisers) among adults in Great Britain

TOXBASE enquiries includes user sessions and page loads; accesses on the TOXBASE iOS App are not included as this was only launched in 2015 and accounts for <2% of enquiries.

While the number of reported poisonings has declined somewhat, at this stage it is not possible to attribute the decline to the introduction of new safety regulations in May 2016. It may be that healthcare professionals are now more familiar with managing EC-related exposures and feel less need to consult NPIS for advice.