Key messages

- The NICE guidelines on smoking harm reduction state ‘Nicotine inhaled from smoking tobacco is highly addictive. But it is primarily the toxins and carcinogens in tobacco smoke – not the nicotine – that cause illness and death. The best way to reduce these illnesses and deaths is to stop smoking’. However, for those who are unwilling or unable to stop smoking the NICE guidance ‘recommends harm-reduction approaches which may or may not include temporary or long-term use of licensed nicotine-containing products.’ The recommendation to use ‘licensed nicotine-containing products’ is to ensure the general public are directed to alternatives that are provably safer and efficacious in helping smokers cut down or quit. It is also imperative that such products are of high and consistent quality and importantly socially acceptable to smokers and those around them.

- Existing marketed licensed nicotine replacement therapy (NRT) products have failed to provide an adequate physiological and psychological alternative to the smoking habit which has led to the uptake of unlicensed e-cigarettes. The public health community now recommends that e-cigarettes are a safer smoking alternative, some 95% safer according to a report issued by Public Health England (PHE), a statement for which there is no conclusive evidence.

- There is, however, a licensed product that in clinical trial and consumer tests, does compete with cigarette smoke in nicotine delivery and in consumer acceptance. Voke is a licensed NRT developed in the UK. In clinical trial, the speed of nicotine absorption achieved by Voke led the MHRA to infer delivery was the result of pulmonary absorption, that is, delivery similar to that of smoking. Voke has also been designed to mimic many of the smoking behaviours and cues that smokers seek and find difficult to give up.

- Unlike e-cigarette vapour, Voke’s formulation is unheated and has met all aspects of regulatory requirements. The difference offered by Voke is a major advance in products licensed to help smokers reduce, replace or stop smoking.

- Plans for the availability of Voke in the UK in 2019 are currently being developed. Healthcare professionals will be able to recommend Voke to patients in the knowledge that it has been through rigorous medicines protocols. Voke will be prescribable.

- The heating of nicotine liquid changes its composition. The effect on the body of heating flavour components is well understood in relation to foodstuffs. The same levels of research and knowledge are not available for flavours blended with nicotine and inhaled rather than ingested. What we inhale can have significant health implications and should not be taken lightly.

- A well-established medicines regulatory regime exists covering the development, manufacture and ongoing marketing of licensed products. The notification provisions introduced by The Tobacco Products Directive do not include verification of the quality of ingredients used and the consistency of manufacture of the more than 30,000 products already listed.

- Statements by PHE that e-cigarettes are, to a high degree, safer than smoking are premature.

- Consumer safety must be paramount. Any relaxation of product regulation for e-cigarettes could risk current safety levels and discourage any further investment in the design, development and introduction of new and improved licensed smoking cessation products.

- Any relaxation in the marketing regulation of e-cigarettes could undermine attempts to promote licensed cessation alternatives to smokers and suggest to consumers that there is little difference between e-cigarettes and licensed products.
Introduction

1. Kind Consumer Limited is a UK-based healthcare company which focuses on developing novel inhalation technologies to address tobacco harm reduction. The company was founded in 2006 by Alex Hearn, a British inventor and entrepreneur based in London. In late 2010 the Company agreed an exclusive development and distribution agreement with Nicoventures Limited (later renamed Nicovations Limited) a wholly owned subsidiary of British American Tobacco plc. In September 2014 Kind Consumer received a product licence for the Company's proprietary nicotine inhaler (Voke Inhaler 0.45mg) for General Sale from the UK Medicines and Healthcare products Regulatory Agency (MHRA).

2. In January 2017 following a number of postponed and aborted launch schedules due to manufacturing failures, the development and distribution agreement with Nicovations Limited was terminated with all intellectual property, manufacturing, marketing and branding rights awarded to Kind. The necessary refinements to the manufacturing process for mass manufacture have now been devised and final stage investment is being gathered for a planned product launch in early 2019.

Speed of nicotine absorption

3. Nicotine from a smoked cigarette will reach the brain in as little as 7 seconds after inhalation. Since a typical smoker takes 10 puffs on each cigarette, a person who smokes a pack of cigarettes a day (20 cigarettes per pack) will receive 200 doses of nicotine daily. The smoker craves those nicotine spikes and the speed of delivery of nicotine plays a significant role in control of cravings. Nicotine absorbed into the blood through the lungs gives a rapid hit. Known as pulmonary absorption, it is what designers of nicotine delivery devices have hoped to achieve and has been recognised in Voke. This is a first for a nicotine replacement therapy and, more generally, a nicotine product.

4. The speed of nicotine delivery found in Voke, is not matched in e-cigarettes. In a recent research study conducted by Reynolds America, published in June 2017, which compared nicotine absorption through its Vuse Solo e-cigarette with that of cigarettes and nicotine gum, it found Vuse Solo to be closer to nicotine gum than combustible cigarettes.

The habit of smoking

5. ‘In addition to the repeated dosing of actual nicotine, certain behaviours, such as bringing the cigarette from hand to mouth at the same frequency, co-occur with the dosing. Other behaviours, such as smoking the first cigarette of the day or smoking after a meal, while on the phone, or driving a car, also become associated with smoking and reinforce continued use. As people progress from the action to the maintenance stage, smoking becomes conditioned and connected to more and more behaviours or becomes more firmly connected to specific times, events, and experiences’.

6. Since 2011 the ongoing Smoking Toolkit Study has monitored the growth in electronic cigarette use and the accompanying reduction in use of licensed nicotine products and prescription medication.

7. Although e-cigarettes in their use, involve a different range of behaviours which have become an acceptable alternative for some smoking habits, they cannot deliver the required speed of nicotine hit. Instead they have become long exposure “grazing” products that build nicotine levels over time.

8. The thinking behind conventional NRT was that it should not assume a similarity to smoking, rather the products should provide a remedial therapy. Voke ignores this thinking and has been designed to be consumer acceptable, replicating many of the behaviours associated with the
smoking habit as well as delivering nicotine at speed, representing a consumer acceptable alternative for the smoker that meets the high standards required of medicines. Importantly, with no visible exhalation and virtually no odour, Voke’s discreetness is equally socially acceptable to those around smokers.

9. The popularity of e-cigarettes, in the absence of acceptable NRT products, should not allow consumer pressure to subsume the requirement for health and safety. Nor should pressure from vapour manufacturers, who are now increasingly dominated by big tobacco.

Tobacco harm reduction

10. In 2007 the Royal College of Physicians first promoted the principle of harm reduction in nicotine addiction. Their argument was integrated into national tobacco control strategies. At about the same time, e-cigarettes began to appear in, what became, a wholly unregulated consumer driven world.

11. We are now at the stage where PHE and leading healthcare professionals support the view that e-cigarettes are up to 95% safer than smoking. For the first time, in 2017, e-cigarettes were actively promoted as part of the government’s Stoptober campaign. In its Smokefree website, the Department of Health states that e-cigarettes are ‘tightly regulated for safety and quality’. However, there has to be a distinct fear that, with this kind of endorsement, e-cigarettes will assume a level of safety that is currently not substantiated by consistent, long-term research.

12. It is also accepted by healthcare professionals and the Department of Health that licensed products represent the only real assurance of safety, quality and efficacy, but this message is in danger of being lost. Voke has attracted considerable investment and research has shown the potential benefit it could offer. Further investment is dependent upon a regulatory environment for licensed nicotine replacement therapies that supports their development and marketing, and upholds the difference with e-cigarette regulation.

Voke

13. Voke relieves and/or prevents craving and nicotine withdrawal symptoms associated with tobacco dependence. Voke is indicated to aid smokers wishing to quit or reduce prior to quitting and as a safer alternative to smoking for smokers and those around them. Each charge of the Voke stick contains 0.45mg of nicotine delivered in 6-8 puffs. This nicotine dose is approximately one twentieth of the nicotine dose in a conventional tobacco cigarette, yet the effective craving relief helps smokers control their nicotine intake. The Voke formulation is primarily a mix of nicotine and HFA134a (the same propellant used in common asthma inhalers) but also contains small amounts of ethanol, saccharin, levomenthol and propylene glycol. Voke has been designed to efficiently deliver an inhalable particle size for lung absorption – a first for NRT. The device does not use heat and does not change the composition of the aerosol.

14. The Voke formulation does not contain acetaldehyde, acrolein, formaldehyde – key e-cigarette vapour emissions which must be notified to the MHRA. Nor does Voke contain the other chemicals in emissions that, depending on the particular device / liquid combination and the toxicological assessment, have to be notified including diethylene glycol, ethylene glycol, diacetyl, pentane 2,3 dione and tobacco specific nitrosamines.

15. When the Voke stick is charged, a valve transfers the nicotine formulation into the stick. The stick itself is breath activated and when the user draws and inhales on it, they feel a cool burst in the mouth and at the back of the throat. As the nicotine aerosol is inhaled, it is quickly absorbed to reduce cravings. Once inhaled no vapour is seen on exhalation. As a licensed medicine, Voke will be prescribable.
Voke’s implications for smoking cessation

16. To study the potential impact of Voke’s improved nicotine delivery on smoking habits, a 13-week market test among smokers was conducted. The study found that up to 50% of participants said they would probably or definitely buy Voke. The average substitution intention of those expressing a definite intention to buy in the coming month, after 13 weeks, was 71%. Smokers’ initial response to Voke, once the product was tried, was reasonably consistent with 59% of responders intending to buy after their initial trial and maintaining their intent throughout the 13 week exercise.\(^8\) The test results are a strong indication of smoker interest in Voke as a licensed alternative to combustible cigarettes.

The weakness in current e-cigarette regulation

17. The growth of e-cigarettes has in part been due to the use of flavours in the e-liquid. In the absence of a European safety standard, suppliers have tended to refer to the US standard ‘generally recognized as safe’ (GRAS) under the US 1958 Food Additives Amendment to the Federal Food Drug and Cosmetic Act. According to the Flavor and Extract Manufacturers Association, ‘None of the primary safety assessment programs for flavors, including the GRAS program sponsored by the Flavor and Extract Manufacturers Association of the United States (FEMA), evaluate flavor ingredients for use in products other than human food. FEMA GRAS status for the use of flavor ingredients in food does not provide regulatory authority to use flavor ingredients in Electronic Nicotine Delivery Systems (ENDS), or any tobacco products in the U.S. ...The manufacturers and marketers of ENDS, and all other flavored tobacco products, and flavor manufacturers and marketers, should not represent or suggest that the flavor ingredients used in these products are safe because they have FEMA GRAS status for use in food because such statements are false and misleading’.\(^9\)

18. In 2015 a study established the presence of diacetyl, associated with bronchiolitis obliterans and other severe respiratory diseases, in many of the flavoured e-liquids tested\(^10\). This report led the
Written evidence submitted by Kind Consumer Limited (ECG0026)

NHS to state, ‘More information is needed on the potential causal link between these chemicals and lung disease, particularly the doses at which any damage might occur’. The NHS response also suggested that, ‘Many e-cigarette users may be asking themselves whether they should stop vaping. This study only provides indirect evidence of a risk linking chemicals in e-cigarettes to lung disease, but, if this is true, the consequences could be serious. At present, there are more questions than answers. There’s little doubt not smoking tobacco or e-cigarettes is the best way to reduce your risk.’

19. The WHO in its review of e-cigarettes states, ‘There are no studies with long-term follow-up. The longest follow-up period is two years. As most smokers have no or few and mild symptoms, for example a mild cough, for decades, potential serious adverse effects of e-cigarette use should not be expected in short-term studies.’ Among its considerations, it warns that a compound found in a harmless concentration might interact with other compounds of low concentration creating harmful effects and that with no standard vaping machines or testing methodologies, it will be difficult to make comparisons between studies. It is suggested that, ‘the risk seems to depend not only on the brand and batch of e-cigarette or e-fluid, but also on the flavour, the heating of the e-cigarette, how dirty or worn the e-cigarette is, the vaper, the vaporizer, and factors still unknown.’

20. This point was also emphasised in a 2016 study by the European Commission Joint Research Centre which considered a key issue that would face regulators following the introduction of the Tobacco Products Directive. The study stated that, ‘The wide variety of products available and the high level of customisation with varying design, type of heating elements, pressure drop, batteries and the huge choice of e-liquids, make the development of such (research) methods and the associated standardised testing conditions particularly challenging’.

The assurance provided by a medicines licence.

21. According to the MHRA, ‘The principal aim of the Agency is to safeguard the public’s health. It does this by making sure that medicines and medical devices—from painkillers to pacemakers—work properly and are acceptably safe; and by responding promptly when new concerns come to light. No product is completely free of risk but sound evidence underpins all the MHRA’s decisions to ensure that these risks are minimised. Licences for medicines are granted only when a product meets high standards of safety and quality and works for the purpose intended. ...The regulatory system also imposes rigorous standards on medicines manufacturers and wholesale dealers who trade in them’.

22. The regulatory system introduced by the Tobacco Products Directive is of a deliberately lower standard. While it is understood that this move was designed not to inhibit availability and innovation, it also fails to acknowledge the unknowns that exist around the inhalation of the array of heated chemical blends in e-liquids, their impacts at different temperatures and the inconsistencies that may arise during manufacture.

23. To date some 30,000 products have been notified to the MHRA but no further checking takes place unless concerns arise that are passed to the regulator by email or through the Yellow Card scheme, neither of which will be intuitive to the average consumer.

Recommendations

At Kind Consumer, we therefore:

24. Urge the Science & Technology Committee to recommend that there should be no relaxation in e-cigarette regulation under pressure from e-cigarette manufactures and until much more is known about their long-term health impacts through consistent, standardised testing.
25. Recommend that the public health community should be encouraged to desist from suggesting e-cigarettes provide a markedly safer alternative when so little proof exists and, therefore, that all those offering Stop Smoking Services should always recommend licensed NRT products first, as the only alternatives with proven safety, quality and efficacy

26. Recommend that marketing restrictions on e-cigarettes should remain in place, especially to allow consumers to recognise the material difference between licensed NRT products and e-cigarettes.

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1 MHRA UK Public Assessment Report Voke 0.45mg nicotine inhaler
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4 www.smokinginengland.info/lateststatistics October 2017
6 E-cigarette working group discussion paper on submission of notifications under article 20 of Directive 2014/40/EU, Chapter 3 – Emissions from Electronic Cigarettes
7 http://www.kindconsumer.com/products/voke-inhaler-technology
8 Extended product usage test, 2013 (n=148)
10 Harvard TH Chan School of Public Health, Flavoring Chemicals in E-Cigarettes: Diacetyl, 2,3-Pentanedione, and Acetoine in a Sample of 51 Products, Including Fruit-, Candy-, and Cocktail-Flavored E-Cigarettes, Environmental Public Health June 2016
12 WHO A systematic review of health effects of electronic cigarettes December 2015
13 European Commission Joint Research Centre, Institute for Health and Consumer Protection, 21027, Ispra, VA, Italy; Correlation of volatile carbonyl yields emitted by e-cigarettes with temperature of the heating coil and the perceived sensorial quality of the generated vapours, International Journal of Hygiene and Environmental Health, 2016
14 MHRA Medicines & Medical Devices Regulation: What you need to know; p2 paras 1,2, p5 para1. http://www.mhra.gov.uk/home/groups/comms-
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