

ASH Scotland MHRA NCP consultation response (MLX 364)

May 2010

Summary:

- ASH Scotland is supportive of the concept of harm reduction for smokers who are unable to cease use of tobacco products
- Evidence on the safety of e-cigarettes is limited - it is highly unlikely that long term use of e-cigarettes will cause harm of the same magnitude as caused by smoking - but documented inconsistencies in product contents and labelling are of concern
- Evidence on the efficacy of e-cigarettes as cessation/nicotine maintenance devices is also limited, but anecdotal report and initial published data shows some promise
- Hence ASH Scotland considers that regulation would have several advantages, both in terms of ensuring consumer safety through consistent manufacture and accurate consumer information and also ensuring e-cigarettes and other NCP can make the best possible contribution to public health as a harm reduction aid, should they be demonstrably safe and effective as a tobacco alternative
- The regulatory approach should be such that it encourages competition within the nicotine replacement market (at the same time as ensuring safety and efficacy), and does not advantage existing pharmaceutical NRT manufacturers through discouraging product innovation
- **In this light ASH Scotland supports MHRA option 2, with the suggestion that sufficient lead in time is provided and that a sufficiently facilitative regulatory framework is implemented to ensure that the market permits access to a wider range of safe, effective and acceptable alternative sources of nicotine**

1. Action on Smoking and Health Scotland (ASH Scotland) welcomes the opportunity to respond to the Medicines and Healthcare products Regulatory Agency's consultation MLX364 on the regulation of nicotine containing products (NCPs). ASH Scotland is an independent Scottish charity working in partnership to protect people from the harm caused by tobacco.

2. Context: Nicotine use in Scotland

ASH Scotland is supportive of the concept of harm reduction for smokers who are unable to cease use of tobacco products entirely. As nicotine is the primary psychoactive component of cigarette smoke that causes tobacco addiction¹ it is important that smokers who are unable

to give up nicotine use are offered less harmful methods of nicotine delivery than that contained in tobacco smoke (which includes over 60 identified carcinogens² in addition to thousands of other chemical compounds). As is well documented³, nicotine itself is a relatively benign drug in the doses administered to the user by tobacco products and pharmaceutical nicotine replacement therapy (NRT), the harm caused by smoking arises almost entirely from exposure to the other compounds present in tobacco smoke.

3. Current clinical guidance on smoking cessation⁴ based on the highest quality research emphasises that best practice in smoking cessation involves setting a discrete quit date after which the individual should strive to maintain total abstinence from tobacco products. As withdrawal from tobacco use may bring with it a range of physical and psychological side-effects⁵ which may undermine the attempt to quit, pharmaceutical nicotine replacement products are often recommended to alleviate the symptoms of withdrawal, which have been repeatedly demonstrated to increase the chance of successful cessation over placebo by 50-70%, regardless of setting⁶.
4. Pharmaceutical NRT products have been demonstrated through clinical trials and observational studies to be generally very safe drugs⁷, with side effects generally localised and specific to the method of delivery used⁸ (e.g. skin irritation where nicotine replacement patches are applied). There is no direct evidence that NRT products are carcinogenic, or that their use increases the risk of other common smoking related diseases in humans⁹. Similarly, the use of nicotine through pharmaceutical products does not appear to provoke cardiovascular events¹⁰, and is approved for use during pregnancy¹¹.
5. Currently licensed nicotine delivery products are usually only used by smokers wishing to give up for 8 or more weeks beyond their target quit date, though many are indicated as safe for use for longer periods – potentially for many months¹². ASH Scotland believes that, as long as the evidence on long term NRT use continues to suggest the risks are extremely low (and many orders of magnitude safer than continued smoking), smokers should be permitted easy access to alternative sources of nicotine.

6. **Electronic cigarettes and other NCPs**

In this context, ASH Scotland is supportive of alternative nicotine delivery systems for smokers seeking to reduce tobacco use, provided they can be demonstrated as a safe and effective means of delivering nicotine to the body. As electronic cigarettes (and to a lesser extent other currently unregulated NCPs like topical gels) are gaining increasing popularity, it is important these products are held to the same standards as existing nicotine-delivering products to ensure safety for the consumer.

7. The prevalence of electronic cigarettes and other NCPs in Scotland is difficult to judge, as no official survey statistics measure their use. However, ASH Scotland conducted a recent YouGov survey, finding that approximately 7% of adult smokers surveyed have used e-cigarettes (with around 3% still using them)¹³. A trade journal for the tobacco industry reports that e-cigarettes have begun to gain increasing popularity in the UK from 2007 onwards following the introduction of smoke-free indoor air legislation, with one company estimating current sales of *'10,000 electronic cigarette kits per month and around 250,000 nicotine*

cartridges¹⁴. E-cigarettes appear to be increasingly widely advertised, with promotional materials appearing in the retail trade press¹⁵, and widely throughout the internet^{16,17}. The growth of an alternative nicotine delivery method that is satisfactory to smokers has the potential to be of benefit to public health, providing that such products can be demonstrated to be acceptably safe and effective in their intended manner of use.

8. There is anecdotal evidence from communities of e-cigarette users¹⁸ that some individuals find the e-cigarette to be a satisfactory alternative to continued smoking. This is highly plausible as such devices mimic the behavioural aspects of smoking (e.g. holding a device in the hand, having control over dosage, inhalation of vapour into the respiratory system) as well as delivering the pharmacological effects of nicotine. A recent publication¹⁹ of the results of an internet survey of e-cigarette users echoes this observation, with respondents reporting that the positive outcomes from e-cigarette use included their usefulness to quit smoking, though this was from a small, self-selecting population. It is possible that there are unsatisfied users of e-cigarettes whose anecdotes have not been publicised as widely however. As a relatively new product on the market (and one that is under constant product development and evolution), to date there is only limited published scientific evidence on both the safety of such devices and their efficacy as a cessation aid, and the little that exists may not be generalisable to all products currently on the market (particularly recent generations of e-cigarettes).

9. What is currently known about e-cigarettes:

- there is no evidence regarding the health effects of long term use²⁰, though it is almost certainly many times less hazardous than continued smoking
- limited testing of two brands by the Food and Drug Administration in the USA found low levels of tobacco specific nitrosamines and impurities in all e-cigarettes cartridges, also identifying diethylene glycol (a potential human toxin) in one cartridge tested²¹
- tests carried out by the manufacturers in response to the FDA analysis found no evidence of carcinogenic N-nitrosamines in their sample²²
- a report from a Greek research institute found no evidence of polycyclic aromatic hydrocarbons in its toxicological analysis of electronic cigarettes²³
- as part of an independent clinical trial²⁴, e-cigarettes were found to suppress cravings less effectively than cigarettes and did not increase plasma nicotine levels significantly²⁵
- however, a further trial found that a Ruyan brand e-cigarette containing nicotine alleviated the desire to smoke as well as a conventional Nicorette nicotine inhalator, performed significantly better than a placebo e-cigarette, and was rated more pleasant to use than the inhalator.²⁶

10. E-cigarette safety

From the limited evidence available at present, it would seem that e-cigarette products, as tested, may be liable to inconsistencies in manufacturing process whereby the composition of

the vapour delivered to the user could vary from brand to brand²⁷. As smoking of tobacco is a uniquely harmful pursuit, it is highly unlikely that any e-cigarette - when used as intended - could be as harmful as continued tobacco use. However, consumers should be protected from potentially harmful variance in product composition, accompanied by adequate product information.

11. Currently the product safety of e-cigarettes in the UK is controlled by general product safety legislation and the Chemicals (Hazard Information & Packaging for Supply) Regulations 2002 (CHIP) which require e-cigarettes to be supplied with child-resistant packaging and toxic warning labels. LACORS (the Local Authorities Coordinators of Regulatory Services) has carried out testing on several brands of e-cigarettes - so far many have failed to comply with the requirements of CHIP^{28,29}. In Scotland, tests carried out by Highland Council Trading Standards Officers in 2008 led to the withdrawal from sale of e-cigarette brands in Inverness³⁰ due to concerns that inadequate controls and warnings could potentially lead to accidental child poisoning.
12. As e-cigarettes are routinely advertised as a substitute for smoked tobacco in places where smoking is prohibited³¹, it is important to ensure that the emissions produced are safe for the bystander in addition to the user. In contrast to exposure to sidestream and exhaled mainstream smoke from conventional cigarettes which increases the risk of lung cancer in heart disease in non-smokers³², propylene glycol is the main component of exhaled e-cigarette vapour which appears to be relatively benign with no evidence that it is a carcinogen or indication that is significantly toxic upon inhalation³³. However, given the apparent manufacturing differences between brands in the limited analyses conducted to date³⁴, product emission should be considered during regulation to ensure the emission of each product granted marketing authorisation is safe for non-users.
13. Regulation of the product by the MHRA would therefore be advantageous, ensuring that manufacturers comply with a uniform standard so the consumer has a guarantee that the product is acceptably safe. These standards should have parity with those that apply to existing NRT products.
14. **Efficacy as a cessation aid**
Evidence on the efficacy of e-cigarettes as a stop-smoking aid is extremely limited. Although a study has found that the brands of e-cigarettes tested did not increase nicotine plasma levels significantly over the period studied, it is likely that (as is the case with other NRT products) increases in plasma nicotine levels will take more time to reach detectable levels than is the case with conventional cigarettes^{35,36}. Initial trial data³⁷ comparing an e-cigarette with a conventional NRT inhalator shows promise regarding the efficacy of the e-cigarette as an alternative to smoking, and should be followed by more extensive trials.
15. There is a concern that, if unlicensed NCPs do not adequately alleviate withdrawal symptoms, belief in the efficacy of alternative (non-tobacco) sources of nicotine in the user may be undermined and the likelihood of future quit attempts may be reduced. Anecdotal reports of e-cigarette user satisfaction and the emerging scientific literature make it seem as though this is unlikely to be the case, but further evidence is needed. Product regulation

through the MHRA that ensures e-cigarettes have comparable efficacy to existing NRT products, in addition to being safe to use, will reduce this risk.

16. Conclusions

E-cigarettes and other NCPs fall into a regulatory gap in many countries, an undesirable situation given the well-documented harms of tobacco use and the positive contribution acceptable alternative sources of nicotine delivery may be able to make to public health. The published evidence base on NCPs is limited: what can be said with some certainty is that e-cigarettes are likely to be much less harmful than tobacco, and that there are early indications they can be a satisfactory alternate source of nicotine for addicted smokers. However, discrepancies in product characteristics across brands (most likely arising from inconsistencies in the process of manufacture), inadequate product information and lack of adherence to existing safety legislation that is intended to govern these products are sources of concern. In this light, ASH Scotland supports the World Health Organisation Study Group on Tobacco Product Regulation's recommendation that e-cigarettes should be regulated as nicotine delivery devices³⁸ and the UK Department of Health's position, as published in February 2010, that all non-tobacco products which contain nicotine should be regulated under medicines safety regulation³⁹.

17. However, the relatively high cost, limited availability (when compared to tobacco products) of pharmaceutical NRT - combined with dissimilarities in the method of their use compared to smoking - mean that, to date, most UK smokers do not utilise them in their attempt to quit despite their demonstrated efficacy in clinical trials. Hence it is important that the regulatory framework in place to control emerging NCPs should ensure that it does not disadvantage new entrants to the market through overly burdensome regulation, though safety and efficacy should of course be assured. E-cigarettes simulate behavioural aspects of smoking closely which leads to concerns they may, under some circumstances, act as a gateway to nicotine or tobacco use for some non-users or impede cessation for some who would otherwise have quit completely. Hence it is important that the regulation of marketing for e-cigs and other NCPs emphasise their intended use as tobacco cessation aid/tobacco alternative intended for existing tobacco users, not as a recreational nicotine product. As regulating by function (rather than by claim) is a departure from routine MHRA practice, it is reasonable to also depart from standard practice by allowing a period of lead-in for manufacturers of e-cigarettes and other NPC to apply for Marketing Authorisation. ASH Scotland would further suggest that the regulatory process for nicotine products is designed with care to ensure that the undesirable status quo (most nicotine users using the most harmful form of nicotine delivery) is not maintained.

18. ASH Scotland supports option 2; with the suggestion that sufficient lead in time is provided and that a sufficiently facilitative regulatory framework is implemented to ensure that the market permits access to a wider range of safe, effective and acceptable alternative sources of nicotine.

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