International Journal of Drug Policy xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Commentary

Is there any legal and scientific basis for classifying electronic cigarettes as medications?

Konstantinos E. Farsalinos [a], Gerry V. Stimson [b,*]

[a] Onassis Cardiac Surgery Center, Athens, Greece
[b] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom

ARTICLE INFO

Article history:
Received 20 January 2014
Received in revised form 5 March 2014
Accepted 13 March 2014

Keywords:
Electronic cigarette
Medicines regulation
Legal
European Union
Definition of medicine
Court judgements
Nicotine

ABSTRACT

The rapid growth in the use of electronic cigarettes has been accompanied by substantial discussions by governments, international organisations, consumers and public health experts about how they might be regulated. In the European Union they are currently regulated under consumer legislation but new legislation will regulate them under the Tobacco Products Directive. However, several countries have sought to regulate them under medicines regulations. These claims have been successfully challenged in 6 court cases in European states. Under European legislation a product may be deemed to be a medicine by function if it is used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. It is a medicine by presentation if it is presented (e.g. by a manufacturer or distributor) as having properties for treating or preventing disease in human beings. We assess the legal and scientific basis for the claim that electronic cigarettes should be regulated as medicines. We conclude that they are neither medicine by function nor necessarily by presentation The main reason for their existence is as a harm reduction product in which the liking for and/or dependence on nicotine is maintained, and adoption of use is as a substitute for smoking and not as a smoking cessation product. In reality, they are used as consumer products providing pleasure to the user. They are not used to treat nicotine addiction or other disease, but to enable continued use of nicotine. Their use is adjusted individually by each consumer according to his or her perceived pleasure and satisfaction. Gaps in current regulation regarding safety and quality can be met by tailored regulations.

© 2014 Published by Elsevier B.V.

Introduction

Electronic cigarettes have been gaining in popularity in recent years. First introduced into many counties around 2006, there has been a rapid rise in sales: in the US for example sales were valued at $20m US in 2009, and have more than doubled each year to over $1b in 2013 (Natalie Robehmed, 2013). According to Eurobarometer data from 2012, it is estimated that there are seven millions users in Europe (European Commission, 2012a). They can be considered tobacco harm reduction products, in that they provide an alternative less harmful product to tobacco cigarettes (Rodu, 2011). As in any other kind of harm reduction approach, tobacco harm reduction is appropriate for smokers who want to give up smoking but find it hard to give up nicotine due to the limited efficacy and appeal of currently approved therapeutic options to treat nicotine and cigarette dependence. Moreover, there is a substantial proportion of smokers who are unwilling to be deprived of the positive experience of nicotine or the act of using cigarettes but would prefer an alternative product to maintain perceived pleasure but reduce harm (Bell, 2013; Britton & Edwards, 2008).

Current medications consist of nicotine replacement therapies (NRT – mostly in the form of gums and patches), oral medications (bupropion and varenicline) and psychological support. The efficacy of these medicinal products is disappointing. In randomized controlled trials, NRTs have a 1-year success rate of approximately 7%, which is much less when psychological support is not included (Moore et al., 2009). In cohort studies of real world quit attempts over-the-counter use NRT in self-initiated quit attempts confers no advantage over stopping without any aid (Kotz, Brown, & West, 2014). There is no evidence for the effect of NRT at a population level. The efficacy of oral medications is lower than 20% even in well-designed medical studies (Rigotti et al., 2009), while in everyday clinical practice it is considerably lower (Casella, Caponnetto, & Polosa, 2010). Moreover, oral medications are hindered by serious

* Corresponding author. Tel.: +44 020 8332 2127.
E-mail address: gerry.stimson@gmail.com (G.V. Stimson).

http://dx.doi.org/10.1016/j.drugpo.2014.03.003
0955-3959/© 2014 Published by Elsevier B.V.

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003

adverse neuropsychiatric effects (Hays & Ebbert, 2010). As a result, the majority of smokers are unable to quit smoking with currently available methods. Additionally, those who want to continue experiencing the positive effects of the smoking habit are unlikely to use any kind of medication since these do not substitute the pleasure perceived from smoking.

Electronic cigarettes consist of a lithium battery, an atomizer, and a fluid filled cartridge. There is no tobacco and no combustion. The atomizer comprises of a storage part for liquid, a resistance and a wick. The liquid evaporates when heated, by activating the battery part of the device which delivers electrical current to the resistance. There is a huge variability of electronic cigarette devices: small "first generation" devices which look similar to a tobacco cigarette, second generation devices which do not resemble cigarettes and are filled by the user and third generation devices which incorporate adjustable electronic circuits that affect taste and performance. The liquid in electronic cigarettes contains nicotine, propylene glycol or vegetable glycerin, and flavorings. There is a large choice of electronic cigarette liquids, with a wide range of flavorings and nicotine levels from 0 up to 36 mg/ml (and more in some cases). Electronic cigarettes are used similarly to tobacco cigarettes: the user takes puffs of aerosol (instead of smoke) and exhales visible aerosol (that resembles smoke in appearance). The difference with electronic cigarettes is that, instead of combustion which produces the smoke in tobacco cigarettes, the aerosol (commonly referred to as "vapor") is produced by heating the liquid at 5–10 times lower temperatures compared to tobacco cigarettes (Laugesen, 2009).

The introduction of electronic cigarettes has led to considerable uncertainty as to how the devices and their contents should be regulated. In the European Union they are currently covered by 17 EU directives and regulations covering for example general product safety, packaging and labeling, chemical safety, electrical safety and weights and measures. Under new legislation which will take effect in 2016, they will be regulated under the Tobacco Products Directive. Several governments, including the UK, Sweden, Germany and Greece have proposed that they should be regulated as medical products and devices. Medicinal regulation was proposed in the draft European Tobacco Products Directive (European Commission, 2012b) but this was rejected by the European Parliament in favor of a consumer model of regulation. According to a briefing from the Library of the European Parliament (Library of the European Parliament, 2013), there have been 6 court cases successfully challenging the classification of electronic cigarettes as medicinal products (1 in USA, 1 in Estonia, 1 in the Netherlands and 3 in Germany), and additionally a recent case in Hungary. In all these cases, the court rulings prohibited the regulation of electronic cigarettes as medications.

In this commentary we examine the legal and scientific basis for the claim that they are medicines. The commentary originated in expert testimony by one of the authors (KF) to the Court of the 2nd and 3rd district of Budapest, Hungary. The Hungarian Customs seized nicotine-containing products and subsequently an electronic cigarette vendor was prosecuted for violating laws of medicines policy. The Hungarian court ruling determined that electronic cigarettes cannot be classified as medicines.

Legal perspective

According to Article 1 of the *Directive 2004/27/EC of the European Parliament and of the Council* (31 March 2004), a medicinal product is: (a) any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis, or (b) any substance or combination of substances presented as having properties for treating or preventing disease in human beings. The first part defines the medicinal product by *function*, i.e. when the product has specific physiologic functions on the human organism, while the second part defines the medicinal product by *presentation*, i.e. when the product is presented by the manufacturer as having medicinal properties, for example if a manufacturer of a nicotine containing product claims that the product can be used in the treatment of tobacco addiction.

Defining medicinal products by function

The European Union directive makes a very broad and generalized definition of a medicinal product by function. There are many daily activities and products which exert physiological functions. For example, water intake induces significant hormonal and metabolic changes to the human organism, such as interference with the production of aldosterone and anti-diuretic hormone and elevation of urine output by the kidneys. Salt intake has several metabolic and hormonal effects as well as effects in the regulatory system of the volume status and in kidney function. Coffee, other common beverages and energy drinks also have physiological effects on the human body (in fact, some of these products may have effects very similar to smoking). Eating and physical activity have significant physiological effects (such as elevation of heart rate and blood pressure and changes in hormonal status). Smoking tobacco cigarettes or using any other form of tobacco (hookah, chewable tobacco, snus) also has physiological effects on the human body.

In general, every daily activity of humans has significant effects and induces changes to the human organism. It is irrational to accept that physiological alterations in the human body are produced only by medications, since none of the above-mentioned products or activities is medicinal by nature or by definition. Therefore, we suggest that in order for a substance to be considered as medicinal product by function, it should exert physiological effects above or more intense from what is expected from common daily activities and the use of common products. This has been specifically mentioned in the Court of Justice of the European Union in Commission v Germany, stating that: "[. . .] the product concerned, whose effect on physiological functions is no more than the effects of a foodstuff consumed in a reasonable quantity may have on those functions, does not have a significant effect on the metabolism and cannot, therefore, be classified as a product capable of restoring, correcting or modifying physiological functions within the meaning of the second subparagraph of Article 1(2) of Directive 2001/83" (Judgment of the Court, 2007).

Nicotine in tobacco and electronic cigarettes

Liquids used in electronic cigarettes may contain nicotine. Nicotine in these products comes from tobacco leaves and is not produced synthetically. Although synthetic production of nicotine is feasible, to the best of our knowledge no companies currently produce nicotine synthetically because it is significantly more expensive than extracting it from tobacco. The chemical molecule of nicotine in electronic cigarette cartridges is identical to the nicotine present in tobacco leaves. The only process that takes place is the removal of impurities and other chemicals present in tobacco leaves, which means that a cleaner form of nicotine is prepared. Additionally, nicotine is present in other plants, such as eggplants (aubergine), cauliflower, tomatoes and potatoes (Domino, Hornbach, & Demana, 1993). This was probably the main reason why a study on 800 people by the Centers for Disease Control (CDC) in the US found that all participants had detectable cotinine levels in their blood, irrespective of their smoking status (Centers for Disease Control and Prevention, 1993). Nicotine present in electronic cigarettes is identical in nature and molecular composition

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003

to the nicotine present in tobacco cigarettes and in other food products, making it contradictory from a legal perspective to define it as a medication in one case (electronic cigarette) and a consumer product in the other case (tobacco).

Nicotine effects from electronic cigarette use

It might be possible to consider nicotine in electronic cigarettes as a medication if nicotine uptake and subsequent effects were much more intense compared to tobacco cigarettes. However, evidence from a variety of studies evaluating older electronic cigarette devices showed that nicotine absorption from electronic cigarettes is lower than from tobacco (Nides, Leischow, Bhatter, & Simmons, 2014; Vansickel, Cobb, Weaver, & Eissenberg, 2010). Recently, Farsalinos et al. (2014) evaluated the efficacy of new generation devices in nicotine delivery. They found that by using an 18 mg/ml nicotine-containing liquid (which is the most popular nicotine "strength" available in the market) the user cannot get the same amount of nicotine compared to a tobacco cigarette. In reality, smoking one cigarette in 5 min leads to almost 3 times higher blood levels of nicotine compared to using a new-generation electronic cigarette device. Users had to use the new-generation device continuously for 35 min in order to get similar nicotine levels to that from smoking one tobacco cigarette for 5 min, while for first generation devices nicotine delivery was even less efficient. Results indicated that users probably need nicotine at levels of 50 mg/ml in liquids in order to approximate the amount of nicotine delivered from a tobacco cigarette. Similar findings, indicating low nicotine-delivery from electronic cigarettes were observed by another research group (Dawkins & Corcoran, 2014). Therefore, the effects of nicotine from an electronic cigarette are lower than the "normal daily activity" (which is the legal characterization of smoking), due to lower levels absorbed to the blood stream.

Electronic cigarettes and quitting smoking

Another possibility for considering electronic cigarettes as medications from a legal perspective would be if they were used as a short-term method to quit smoking or as a method to gradually reduce and finally eliminate nicotine use and dependence. In this way, they would be used to treat nicotine addiction. This is the way that NRTs are used. The purpose of using pharmaceutical nicotine gums and patches is to gradually reduce nicotine intake until the user completely eliminates its intake. Moreover, according to the Summary of Product Characteristics (SPC) of NRTs in most countries, use of these products should be limited to three months, although there is considerable discussion about their long term use (National Institute for Health and Care Excellence, 2013).

Studies of electronic cigarette consumers show that only a very small minority is able or willing to eliminate nicotine use, even after several months of continuous use (Dawkins, Turner, Roberts, & Soar, 2013; Etter & Bullen, 2011; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Voudris, 2013; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, Spyrou, et al., 2013). In two of the studies (Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Voudris, 2013; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, Spyrou, et al., 2013), only 4.5% and 3.0% of consumers were using zero nicotine liquids after 8 and 12 months of daily electronic cigarette use respectively. Studies of consumers have shown that electronic cigarettes are used as a long term habit (Dawkins et al., 2013; Etter & Bullen, 2011; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Voudris, 2013; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, Spyrou, et al., 2013) that substitutes (partially or completely) for smoking and are not used with the intention to quit nicotine or as a smoking cessation medication. Instead of treating, electronic cigarettes maintain and satisfy the consumer's liking for and/or dependence to nicotine; the advantage of using electronic instead of tobacco cigarettes is solely attributed to receiving nicotine from a less harmful product, by avoiding the products of combustion and the toxins released in tobacco smoke. This cannot be a reason to justify characterization as a medicinal product, in the same way that low-fat milk is not considered a medicinal product just because it is less harmful compared to full-fat milk. This is in direct contrast to pharmaceutical NRTs which are specifically marketed and approved to be used as smoking cessation products and with the purpose to gradually reduce nicotine craving and intake until the user entirely quits taking any nicotine.

Defining medicinal products by presentation

According to the European Directive *2004/27/EC*, a product can be considered medication if it is *presented* as having properties for treating or preventing disease in human beings. In practice, this claim is not made by most electronic cigarette makers and distributors. Electronic cigarettes are mainly marketed by the industry as alternative-to-smoking products, and not as products having therapeutic properties or for treating smoking and nicotine addiction. We cannot exclude the possibility that a company may promote these products as smoking cessation tools for marketing purposes. However, this cannot be a reason to consider them all as medicinal products because there must be definite proof that they have therapeutic properties. Such cases should be more appropriately considered legally as misleading marketing or advertising rather than proof that electronic cigarettes are medications. Paradoxically, the European Directive allows the possibility to characterize electronic cigarettes as medication simply by claiming therapeutic properties (smoking cessation can be considered a therapeutic claim). This is a legal argument that would prevent someone from making arbitrary and misleading claims, unless the product undergoes the full testing requested by the medicinal legislation. The complete substitution of smoking with electronic cigarette use is obviously a desired consequence, but scientifically it cannot be considered by itself justification to classify them as medications.

From a scientific perspective, there are no long-term studies evaluating whether electronic cigarette use has any beneficial health effects to humans (apart from the avoidance of health risks associated with smoking tobacco). Even if future studies show health benefits (which of course would be a welcomed and is an expected finding), it is likely that they will be attributed to a parallel partial or complete substitution of smoking and not to any beneficial effects attributed to electronic cigarette use per se. However, there is a paradox: although the existence of electronic cigarettes is justified due to the health benefits expected for those switching from tobacco to electronic cigarette use, companies are not allowed to promote electronic cigarettes to consumers (smokers) as a potentially less harmful alternative because that would legally consider them as medicinal products by presentation. This is an issue mostly observed in Europe.

In the US, there is currently a definition of modified-risk tobacco products (MRTP); however, the regulatory rules for applying such a label to electronic cigarettes are extremely complex and costly, especially taking into account the huge variability in devices, liquids and flavorings available for electronic cigarette use. Moreover, the MRTP regulation specifically requires evidence about the effects of the product and its marketing on: (a) current users, (b) tobacco use initiation, (c) consumer understandings and perceptions, and (d) the population as a whole (Bell, 2013). Therefore, it seems that this regulation in reality requires evidence that "modified risk" products are not attractive to smokers.

Under current legislation in many European countries, a manufacturer of an electronic cigarette may have the *option* to apply

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003

for a medicines license for an electronic cigarette if a therapeutic claim for the product is made. In reality, they will be using the legal "window" which allows the classification of a product as medication by presentation for two main purposes. First, to overcome nicotine limits which are going to be imposed to electronic cigarettes. The Tobacco Products Directive of the European Union defines 20 mg/ml as the upper limit for electronic cigarettes. Overcoming this limit would make their products more effective as smoking substitutes, due to the low nicotine-delivery potential of electronic cigarettes at the levels dictated by the directive (Farsalinos et al., 2014). Second, to promote the marketing of other electronic cigarette products sold by the company. The medicinal regulation application process is very strict, with extensive and expensive testing that has to be followed, making it unrealistic for a company to request such regulation for more than one or a very limited number of products. Evidence suggests that the success of electronic cigarettes is closely associated with the variability of devices and liquids available for consumers (Farsalinos et al., 2013b). Therefore, medicinal approval for one product is expected to give the company a marketing advantage for other products in their range, for which such approval will not be pursued.

Further considerations

Several scientific aspects of the issue of whether electronic cigarettes should be regulated as medications have been addressed above as relevant to the legal definitional issues. However, there are some additional aspects of electronic cigarette use that distinguishes it from the use of medications.

Nicotine use for pleasure

The popularity of electronic cigarettes is attributed mainly to the fact that they resemble tobacco cigarettes in the way they are used (Barbeau, Burda, & Siegel, 2013; Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Voudris, 2013). The motion (holding the electronic cigarette, hand-to-mouth movement, visible stimuli (visible "smoke" exhaled) and sensory stimulation (throat hit, taste) are experiences which resemble smoking tobacco cigarettes; in fact, such characteristics represent a significant part of the addiction to smoking (Buchhalter, Acosta, Evans, Breland, & Eissenberg, 2005). Users obtain nicotine through inhalation, in a similar way to tobacco cigarettes. Since nicotine is the same molecule that is present in tobacco cigarettes, the user expects to feel the same experience as that obtained from getting nicotine through tobacco. In reality, electronic cigarettes are used as alternative products in order to get similar joy and pleasure as that from tobacco cigarettes, defining them as recreational consumer products. By definition, medicinal products are not made to be used for pleasure and satisfaction, and no medicinal product currently in the market is approved for use in this way.

Use of nicotine products for recreational purposes has been criticized by the tobacco control movement, because it upsets boundaries between good/medicinal and bad/recreational nicotine (Bell & Keane, 2012); however, it is questionable whether this distinction, which in fact "stigmatises" pleasure, is appropriate for a substance that is compatible with the requirements of everyday life (Bell, 2013). In reality, it is the "delivery system" (the cigarette) rather than the drug itself which causes harm (Bell, 2013).

Dosing, medicinal products and electronic cigarettes

An important characteristic of all medications is the need to define a specific daily dose and to have consistent delivery to the organism when used. Every time someone takes a medication, the substance should be consistently released in the same amount and with the same distribution in the human organism. In the case of nicotine intake, a major characteristic is that the user self-titrates (self-adjusts) the intensity and patterns of use according to self-perceived pleasure and saturation (satisfying nicotine needs). In the case of tobacco cigarettes, all smokers have their own unique way of using nicotine, and this is satisfied by adjusting the intensity and frequency of smoking according to self-demand (Benowitz, Zevin, & Jacob, 1998). This characteristic, although not yet proven by medical studies, is also expected to occur in electronic cigarette use. Therefore, it is highly likely that consumers would not accept to be "obliged" to use them in a specific dosage, because this would remove the pleasure element and the self-titration characteristic.

Product choice

Another important characteristic of the electronic cigarette market is the availability of a huge variety of devices, atomizers and liquids, with various nicotine strengths and flavorings for the consumer to choose. Evidence shows that this variability is important for users (Farsalinos et al., 2013b). The ability to choose from different products adds to the positive consumer experience and is reflected in the internet consumer forums and social media groups, in which users exchange views and search for more efficient and pleasing products (Barbeau et al., 2013).

Regulatory options

The "risk" of applying medicinal regulation is that electronic cigarettes will be transformed into another form of pharmaceutical nicotine inhaler; currently there is no need for such a product and it will not be accepted in the same way as electronic cigarettes are currently accepted by consumers. Additionally, strict medicinal regulation will give electronic cigarettes a disadvantage compared to the main competitor, which is the tobacco cigarette. The cost of performing the extensive testing required by medicinal regulation will reduce the range of products available and will make them more expensive (Bates & Stimson, 2013). Additionally, it will negatively affect the evolution and development of new products, which is currently very fast but will be significantly hindered due to the time and resources needed to perform required tests. Moreover, there is the risk that electronic cigarettes will be monopolized by the large tobacco companies who have the funds to make medicines licensing applications (Hajek, Foulds, Le Houezec, Sweanor, & Yach, 2013).

Regulating electronic cigarettes as tobacco products would also be inappropriate. First of all, there is no rationale or scientific basis to classify them as tobacco products: it makes no more sense to argue that nicotine is a tobacco product than to argue that biodiesel is a vegetable product because it is derived from plants. Additionally, regulation as a tobacco product carries the risk of misinforming smokers that the risks associated with electronic cigarette use would be similar to those of smoking tobacco. Currently available evidence overwhelmingly supports the lower risk potential of electronic cigarettes (Farsalinos & Polosa, 2014), and this should be properly communicated to the smokers. Although it is tempting for regulators to integrate electronic cigarettes into an already-established tobacco products regulation, this would be inappropriate, disproportionate and misleading. The main criterion for regulation should be to serve public health in the most efficient way rather than to make the work of the regulators easier.

Regulation is needed in order to promote the quality and safety of the products; however, there are other regulatory pathways by which this can be ensured. Making a separate regulation devoted to electronic cigarettes may be the most appropriate way

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003

to handle this issue. There is a need for specific testing on liquids and vapor, unique for electronic cigarettes. There are already-established standards of purity for liquid ingredients, such as the United States and the European Pharmacopoeia, which should be followed. Testing should be cost-effective and take into account that electronic cigarettes are harm reduction consumer products, substituting combustible tobacco products which have well-known devastating health effects. Therefore, there is no need to prove that they are absolutely safe. Through testing and research, products will become more effective as smoking substitutes and at the same time any potential harm will be minimized. Moreover, regulation should be flexible-enough to address the evolution of new, more efficient products and to maintain the current variability. Finally, rules concerning marketing promotion should be carefully designed in order to educate the public that electronic cigarettes are not a new lifestyle product for everyone to adopt (as was the case of promoting tobacco cigarettes in previous decades) but are developed for the smokers who cannot or do not want to quit with currently approved medications and are now provided with the opportunity to use a less harmful alternative.

Conclusions

In conclusion, currently available scientific evidence and observations of the use of electronic cigarettes by consumers in the real world clearly show that electronic cigarettes are not used as medications and are not used as a treatment – they are neither medicine by function nor necessarily by presentation. The main reason for their existence is as a tobacco harm reduction product (similar to the use of snus in Sweden), which means that the liking for and/or dependence on nicotine is maintained but not treated, and adoption of use is as a substitute for smoking and not as a smoking cessation product. Consumers prefer to use electronic cigarettes because they perceive pleasure without being exposed to the health risks associated with smoking. In this context, they are consumer products directly competing with cigarettes. Nicotine in electronic cigarettes is identical in molecular structure to nicotine in tobacco. Nicotine intake from electronic cigarette cartridges has similar or milder effects compared to nicotine intake from smoking tobacco cigarettes (which can be legally considered as “normal daily activity” for smokers). They are not used to treat nicotine addiction or any other disease, but to maintain continued use of nicotine through a cleaner form compared to combustible tobacco. They are used as a long-term consumer product and their use is adjusted individually by each consumer according to his or her perceived pleasure and satisfaction. On the contrary, no medication is administered without a specific predetermined dosage scheme and no medication is developed or recommended for pleasure and satisfaction. Enhanced regulation of electronic cigarettes is needed to address safety and quality issues not adequately covered by current regulations; however, it would be more realistic and appropriate to develop a regulation specifically designed for electronic cigarettes, addressing the unique aspects of the product and the way they are adopted and used by consumers.

Conflict of interest statement

K.F. is a researcher at Onassis Cardiac Surgery Center. For some of his studies, the institution has received financial compensation from electronic cigarette companies to cover the cost of experiments. A company of which G.S. is a director has received a research feasibility grant from an electronic cigarette company developing a new nicotine delivery device.

References

Barbeau, A. M., Burda, J., & Siegel, M. (2013). Perceived efficacy of e-cigarettes versus nicotine replacement therapy among successful e-cigarette users: A qualitative approach. *Addiction Science & Clinical Practice*, *8*(1), 5.

Bates, C., & Stimson, G. (2013). *Costs and burdens of medicines regulation for e-cigarettes*. Available at http://nicotinepolicy.net/documents/reports/Impacts%20of%20medicines%20regulation%20-%2020-09-2013.pdf Accessed 18.01.14

Bell, K. (2013). Tobacco control, harm reduction and the problem of pleasure. *Drugs and Alcohol Today*, *13*, 111–118.

Bell, K., & Keane, H. (2012). Nicotine control: E-cigarettes, smoking and addiction. *International Journal of Drug Policy*, *23*, 242–247.

Benowitz, N. L., Zevin, S., & Jacob, P., 3rd. (1998). Suppression of nicotine intake during ad libitum cigarette smoking by high-dose transdermal nicotine. *Journal of Pharmacology and Experimental Therapeutics*, *287*, 958–962.

Britton, J., & Edwards, R. (2008). Tobacco smoking, harm reduction, and nicotine product regulation. *Lancet*, *371*, 441–445.

Buchhalter, A. R., Acosta, M. C., Evans, S. E., Breland, A. B., & Eissenberg, T. (2005). Tobacco abstinence symptom suppression: The role played by the smoking-related stimuli that are delivered by denicotinized cigarettes. *Addiction*, *100*(4), 550–559.

Casella, G., Caponnetto, P., & Polosa, R. (2010). Therapeutic advances in the treatment of nicotine addiction: Present and future. *Therapeutic Advances in Chronic Disease*, *1*, 95–106.

Centers for Disease Control and Prevention. (1993). Preliminary data: Exposure of persons aged ≥4 years to tobacco smoke – United States. *Journal of the American Medical Association*, *269*, 852.

Dawkins, L., & Corcoran, O. (2014). Acute electronic cigarette use: Nicotine delivery and subjective effects in regular users. *Psychopharmacology (Berlin)*, *231*(2), 401–407.

Dawkins, L., Turner, J., Roberts, A., & Soar, K. (2013). ‘Vaping’ profiles and preferences: An online survey of electronic cigarette users. *Addiction*, *108*, 1115–1125.

Domino, E. F., Hornbach, E., & Demana, T. (1993). The nicotine content of common vegetables. *New England Journal of Medicine*, *329*, 437.

Etter, J. F., & Bullen, C. (2011). Electronic cigarette: Users profile, utilization, satisfaction and perceived efficacy. *Addiction*, *106*, 2017–2028.

European Commission. (2012a). *Eurobarometer 385. Attitudes of Europeans towards tobacco*. Available at http://ec.europa.eu/public_opinion/archives/ebs/ebs_385_en.pdf Accessed 13.01.14

European Commission. (2012b). *Proposal for a directive of the European Parliament and of the Council 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*. Available at http://ec.europa.eu/health/tobacco/docs/com_2012_788_en.pdf Accessed 18.01.14

Farsalinos, K. E., & Polosa, R. (2014). Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: A systematic review. *Therapeutic Advances in Drug Safety*, *5*(2), 67–86.

Farsalinos, K. E., Romagna, G., Tsiapras, D., Kyrzopoulos, S., & Voudris, V. (2013). Evaluating nicotine levels selection and patterns of electronic cigarette use in a group of vapers who had achieved complete substitution of smoking. *Substance Abuse*, *7*, 139–146.

Farsalinos, K. E., Romagna, G., Tsiapras, D., Kyrzopoulos, S., Spyrou, A., & Voudris, V. (2013). Impact of flavour variability on electronic cigarette use experience: An internet survey. *International Journal of Environmental Research and Public Health*, *10*, 7272–7782.

Farsalinos, K. E., Spyrou, A., Tsimopoulou, K., Stefopoulos, C., Romagna, G., & Voudris, V. (2014). Nicotine absorption from electronic cigarette use: Comparison between first and new-generation devices. *Scientific Reports*, *4*, 4133.

Hajek, P., Foulds, J., Le Houezec, J., Sweanor, D., & Yach, D. (2013). Should e-cigarettes be regulated as a medicinal device? *Lancet Respiratory Medicine*, *1*, 429–431.

Hays, J. T., & Ebbert, J. O. (2010). Adverse effects and tolerability of medications for the treatment of tobacco use and dependence. *Drugs*, *70*, 2357–2372.

Judgment of the Court of 15 November 2007, Commission of the European Communities v Federal Republic of Germany, Case C-319/05 (paragraph 68).

Kotz, D., Brown, J., & West, R. (2014). ‘Real-world’ effectiveness of smoking cessation treatments: A population study. *Addiction*, *109*(3), 491–499.

Laugesen, M. (2009). *Ruyan® E-cigarette Bench-top tests. Society for Research on Nicotine and Tobacco (SRNT) Dublin, Poster 5–11*. Available at http://www.healthnz.co.nz/DublinEcigBenchtopHandout.pdf Accessed 08.01.14

Library of the European Parliament. (2013). *Library briefing: E-cigarettes*. Available at http://www.europarl.europa.eu/eplibrary/Electronic-cigarettes.pdf Accessed 18.01.14

Moore, D., Aveyard, P., Connock, M., Wang, D., Fry-Smith, A., & Barton, P. (2009). Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: Systematic review and meta-analysis. *British Medical Journal*, *338*, b1024.

Natalie Robehmed. (2013). *E-cigarette Sales Surpass $1 Billion As Big Tobacco Moves In.* Forbes. Available at http://www.forbes.com/sites/natalierobehmed/2013/09/17/e-cigarette-sales-surpass-1-billion-as-big-tobacco-moves-in/ Accessed 13.01.14

National Institute for Health and Care Excellence. (2013). *Tobacco-harm-reduction approaches to smoking: Guidance*. Available at http://www.nice.org.uk/nicemedia/live/14178/63996/63996.pdf Accessed 28.02.14

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003

Nides, M. A., Leischow, S. J., Bhatter, M., & Simmons, M. (2014). Nicotine blood levels and short-term smoking reduction with an electronic nicotine delivery system. *American Journal of Health Behavior*, *38*, 265–274.

Rigotti, N. A., Pipe, A. L., Benowitz, N. L., Arteaga, C., Garza, D., & Tonstad, S. (2009). Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: A randomized trial. *Circulation*, *121*, 221–229.

Rodu, B. (2011). The scientific foundation for tobacco harm reduction, 2006–2011. *Harm Reduction Journal*, *8*, 19.

Vansickel, A. R., Cobb, C. O., Weaver, M. F., & Eissenberg, T. E. (2010). A clinical laboratory model for evaluating the acute effects of electronic cigarettes: Nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiology, Biomarkers & Prevention*, *19*, 1945–1953.

Please cite this article in press as: Farsalinos, K. E., & Stimson, G.V. Is there any legal and scientific basis for classifying electronic cigarettes as medications? *International Journal of Drug Policy* (2014), http://dx.doi.org/10.1016/j.drugpo.2014.03.003