

## Commentary on Goniewicz *et al.* (2014): If wisely regulated, electronic cigarettes can make cigarettes obsolete

The most original result of the study by Goniewicz *et al.* is that, for e-cigarettes that contained 18–24 mg of nicotine per ml, nicotine levels in the cartridges were not correlated with nicotine levels in the vapour [1]. In addition to nicotine levels in the vapour, several factors determine nicotine levels in the brain of e-cigarette users: the number and volume of puffs, the duration of apnoea between inspiration and expiration, nicotine metabolism, etc. This has important consequences for regulation, as it indicates that regulating the nicotine levels in e-liquids or even in the vapour has little relevance. Paradoxically, the European Union (EU) prohibits cigarette manufacturers to advertise tobacco cigarettes based on nicotine levels in smoke (in particular, they cannot describe cigarettes as 'light'), because these levels are irrelevant and misleading. Now the EU wants to regulate e-cigarettes based on nicotine concentrations in e-liquids. This effort is misguided. A third of regular e-cigarette users use e-liquids with higher levels than the 20 mg/ml limit currently debated in Brussels [2], and heavy smokers may not switch to e-cigarettes if they are denied access to high-nicotine e-liquids. In fact, current e-cigarettes do not deliver enough nicotine, nor do they deliver it quickly enough to the blood and brain. Better products are needed because, currently, only 12–14% of smokers who try e-cigarettes convert to daily vaping [3,4]. This figure is too low, and the public health potential of e-cigarettes will not be realized if conversion rates do not increase. Manufacturers need to invest more in research, in order to more effectively control the pharmacokinetics of nicotine delivered via e-cigarettes. In future, the e-cigarette market will be dominated by the manufacturers who best control the nicotine delivery to the blood and brain. This can be achieved by controlling the pH of vapours, increasing the proportion of freebase nicotine, controlling the size of droplets to ensure deposition in the lung alveoli or educating users to hold their breath after inhalation. At the dose used by smokers, users of nicotine medications and vapers, nicotine is not toxic but, of course, e-cigarettes might be addictive if their pharmacokinetic profile is improved. However, this is unlikely to become a public health problem. As a comparison, a large amount of nicotine gums are sold to people who use them compulsively (i.e. former smokers who quit a long time ago), rather than to recent quitters [5–7]. Long-term use of nicotine gums is not dangerous, nor is it a public health problem [8]. Conventional definitions of addiction include two elements (compulsive use and adverse effects). The

consequences of long-term vaping have yet to be studied, but no serious adverse event was reported in clinical studies with 6–12 months of follow-up [9,10]. Because vaping has no known adverse consequences, the term 'addiction' is not suited to describe compulsive use of e-cigarettes, no more than it applies to compulsive use of nicotine gums. Regular use of e-cigarettes in never smokers has not been reported so far in the peer-reviewed literature, and e-cigarettes are not a gateway to smoking (they are a gateway out of smoking).

Current laws authorize nicotine only in smoked tobacco (snus is banned in the EU except in Sweden) and in nicotine medications. Because nicotine medications are not very appealing and are seldom used as a long-term alternative to tobacco, people who need nicotine are forced by current laws to smoke tobacco. These laws are responsible for a public health disaster (700 000 tobacco-related deaths in the EU each year) and they have to change. The debate on the place of new nicotine products in society and in the law (including products that heat tobacco instead of burning it) is among the most important public health debates in recent decades. Applying rules to e-cigarettes designed initially for medicines and tobacco would be disproportionate, and have serious adverse consequences for public health. Wise, proportionate regulation of e-cigarettes is needed, and such regulation can only be achieved if all stakeholders are involved, including vapers, manufacturers and scientists, not just technocrats and regulators. The next months will see the regulation of e-cigarettes in the EU and the United States. This is a crucial moment, a narrow window of opportunity. If wisely regulated, e-cigarettes can make cigarettes obsolete. The stakes are high, and we need to play it right.

### Declaration of interests

J.F.E. was reimbursed by an e-cigarette manufacturer for travelling to London and China.

**Keywords** E-cigarette, electronic cigarette, electronic nicotine delivery devices (ENDS), nicotine, smoking, tobacco.

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