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# Introduction to tobacco control supplement

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**ABSTRACT**

Electronic cigarettes (e-cigarettes) have recently gained significant attention in the marketplace and in the media. However, limited information is available about the worldwide impact of e-cigarettes; most public health officials are calling for more data so they can more fully understand the potential risks and benefits of e-cigarettes in order to inform regulatory action. In the USA, e-cigarettes that are marketed as tobacco products are not currently regulated by the Food and Drug Administration (FDA). However, having a continuum of nicotine-containing products that cross jurisdictional lines within the FDA in the future would create the potential (and the need) for a comprehensive nicotine strategy at the FDA. As part of developing the most appropriate approach to e-cigarette regulation, FDA Center for Tobacco Products scientists have been reviewing the available literature to determine the state of e-cigarette knowledge and have identified research areas that could be addressed. This supplement provides a summary of the current knowledge and research gaps pertaining to e-cigarettes with regards to product design, chemistry and toxicology of e-liquid and aerosol constituents, human factor-based risk factors, abuse liability, clinical pharmacology and human health effects, paediatric issues, and environmental issues.

**DISCUSSION**

Electronic cigarettes (e-cigarettes), the most common type of electronic nicotine delivery system (ENDS), have recently gained significant attention in the marketplace and in the media. E-cigarettes, initially developed in China, are now widely available in the USA and many countries internationally and can be purchased via the internet and in retail settings. Awareness of e-cigarettes among US adults more than doubled from 2009 to 2011,<sup>1</sup> and sales of these products has increased rapidly. Industry analysts expected e-cigarette sales to double by the end of 2013 with sales of approximately \$1.7 billion and consumption to surpass traditional cigarettes within the next 10 years.<sup>2–4</sup> Academic researchers have been directing attention towards e-cigarettes as a recreational tobacco product and as a potential therapeutic product to aid with smoking cessation. A recent editorial in *The Lancet* discusses the complexities in balancing the need for a less harmful way to offer nicotine delivery to current users of combusted tobacco products without increasing initiation of nicotine addiction in youth and young adults.<sup>4</sup>

Global attention has been drawn to the rapid rise in availability and use of this heterogeneous group of ENDS products. Limited data are available about the worldwide impact of e-cigarettes. The WHO Study on Tobacco Product Regulation addressed regulation of ENDS in its 2010 report<sup>5</sup> and the

WHO Tobacco Free Initiative released a statement in July 2013 recommending that consumers should be strongly advised not to use any ENDS products until a product is deemed safe, effective (as a smoking cessation aid) and of an acceptable quality by a competent regulatory body.<sup>6</sup> Countries differ in their approach to e-cigarette regulation and have instituted a wide variety of policies relative to e-cigarette sale or use. Most public health officials are also calling for more data so they can more fully understand the potential risks and benefits of e-cigarettes in order to inform regulatory action.

In the USA, e-cigarettes that are “customarily marketed tobacco products” are not currently regulated by the FDA.<sup>7</sup> State and local regulatory authorities also contribute to public health policies impacting the availability and use of these products. As of December 2013, 25 states have laws restricting the sale of e-cigarettes to minors and 6 states have enacted some form of restrictions on e-cigarette use in public spaces.<sup>8</sup> E-cigarettes remain largely or completely untaxed. Several states have introduced legislation to address taxation of these products, with industry supporting bills that will prevent e-cigarette taxation.

The US Court of Appeals for the DC Circuit in 2010 issued a decision in the case of *Sottera, Inc v FDA* with regard to e-cigarettes and other products ‘made or derived from tobacco’ and the jurisdictional line that should be drawn between ‘tobacco products’ and ‘drugs,’ ‘devices’ and combination products. The court held that e-cigarettes and other products made or derived from tobacco can be regulated as ‘tobacco products’ under the Tobacco Control Act and are not drugs/devices unless they are marketed for therapeutic purposes.<sup>7</sup> FDA has stated that it intends to issue a proposed regulation that would assert regulatory authority over products that meet the definition of a tobacco product, including e-cigarettes not marketed for therapeutic purposes.<sup>9</sup>

For years, the spectrum of nicotine-containing products in the USA has ranged from cigarettes to nicotine replacement therapy cessation aids. However, with the advent of e-cigarettes and other novel products, there is an increasing diversity of tobacco products. There is now the potential to have products that contain only nicotine derived from tobacco (rather than tobacco itself) to be marketed as tobacco products or as drugs/devices.

Having a continuum of nicotine-containing products that cross jurisdictional lines within FDA (tobacco product vs, for example, cessation aids) creates the potential (and the need) for a comprehensive nicotine strategy at FDA. It also brings into the forefront questions about the potential for the development of nicotine replacement therapies that are more effective at helping tobacco users quit than



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current products. It also raises the possibility of nicotine-containing products that may be chemically and mechanically very similar to cessation aids but that are marketed for recreational use. How these developments affect public health depends upon the products' properties and toxicities, but more importantly, how they are used. Under different scenarios of use, the same product could either benefit or harm public health.

In theory, the scenario with the least potential for population harm is the development of highly acceptable nicotine replacement therapies that are significantly more effective than current products on the market at enabling tobacco users to quit with a short duration of treatment. More effective cessation aids that allow a longer period of use are also likely to benefit population health if the ultimate goal is nicotine abstinence. However, the size of the impact is highly dependent upon the extent to which such products accomplish complete cessation and the extent to which they are used.

'Pure' nicotine products that are marketed for recreational use as tobacco products also have the potential for population benefit to the extent that the adverse health effects from tobacco use disproportionately lie with the other chemicals in the tobacco and in the smoke. Under an optimistic scenario, few additional non-users would initiate tobacco use and/or develop nicotine dependence, many current users who would not have quit would completely switch, few tobacco users who would have quit smoking would delay cessation in favour of dual product use, and few former users would relapse back to nicotine or tobacco use, resulting in a public health benefit. Under a pessimistic scenario, many additional non-users would initiate nicotine use with some progressing to conventional tobacco product use, few current users would completely switch and dual usage with delayed cessation would be the predominant pattern of use, and a significant number of former users would relapse back to tobacco use, resulting in population harm.

The net population impact depends on the number who potentially benefit multiplied by the magnitude of that benefit and the number potentially harmed multiplied by the magnitude of the harm they experience. A goal of a comprehensive nicotine regulatory policy could be to optimise the development and use of nicotine cessation products and to regulate 'recreational' nicotine products in order to maximise the potential benefits (ie, encourage complete substitution to the 'cleanest' products among current users, while minimising initiation of use, delayed cessation or relapse back to tobacco use). Currently, the assessment and development of such a comprehensive regulatory strategy is hindered by the paucity of data noted in the accompanying literature reviews—data on the toxicities of the products and more importantly, data on how these products are being used.

FDA currently regulates cigarettes, cigarette tobacco, roll-your-own tobacco and smokeless tobacco but has indicated its intent to assert its regulatory authority to products that meet the definition of "tobacco product". Under such authority, companies would be required to provide information about the ingredients in the products and the levels of certain chemicals to which users are exposed. In 2011, FDA and National Institutes of Health (NIH) announced a new study, the Population Assessment of Tobacco and Health Study, a longitudinal study that surveys respondents about use of a variety of tobacco products, including e-cigarettes. This study will provide important information on the trajectories of tobacco use among youth and adults; the impact of the availability of novel tobacco products on initiation of dual and polytobacco product use, as well as tobacco use cessation and relapse; and how product use affects exposure to harmful and potentially harmful constituents and,

ultimately, health. Approximately 59 000 people ages 12 years and older are anticipated to enrol in the Population Assessment of Tobacco and Health Study cohort.<sup>10</sup> In addition, FDA has partnered with Centers for Disease Control and Prevention and NIH to expand existing national surveys to track changes in awareness, use, susceptibility and perceptions of e-cigarette use among youth and adults in the USA. FDA is also partnering with NIH to develop research initiatives such as the Tobacco Centers of Regulatory Science to fund tobacco regulatory research, including many projects that directly relate to e-cigarettes.<sup>11</sup> Furthermore, a formal system for reporting tobacco-specific adverse events, including from e-cigarettes, has just recently been established.<sup>12</sup> Product surveillance will assist FDA to identify safety concerns with reported products. Data from these various sources will help start answering the fundamental questions to allow a science-based determination about the likely impact of e-cigarettes on individual and population health and how regulatory actions could ensure that the net effect on public health is most likely to be positive.

In the November 2013 online issue of this journal, Pepper and Brewer systematically reviewed the literature related to growth in awareness and use of e-cigarettes, finding that from 2009 to 2011, e-cigarette use increased from 1% to more than 6%, with use primarily concentrated among current or former smokers. This review forms an important part of the evidence base regarding information about who is using e-cigarettes, and, to some extent, why.<sup>13</sup> Similarly, as part of developing the most appropriate approach to the regulation of e-cigarettes, the FDA Center for Tobacco Products scientists have been reviewing the available literature to determine the state of e-cigarette knowledge and have identified research areas that inform regulation. In particular, this supplement provides a summary of the current knowledge and research gaps pertaining to e-cigarettes with regards to: product design, chemistry and toxicology of e-liquid and aerosol constituents, human factor-based risk factors, abuse liability, clinical pharmacology and human health effects, as well as paediatric issues, and environmental issues.

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