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Tobacco Products Regulatory Office
Tobacco Control Directorate
Controlled Substances and Cannabis Branch
Health Canada
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March 4, 2021

Dear Mr Cook,

Re: Response to the Canadian Consultation on Proposed Concentration of Nicotine in Vaping Products Regulation

I am a professor of public health sciences at Penn State – College of Medicine, and have conducted research on tobacco and health for over 30 years, and been an author on over 150 published papers. Over the past 10 years I have conducted research on electronic cigarettes and developed a widely used measure of the severity of addiction to electronic cigarettes (1). I do not do any paid work of any sort for the tobacco or electronic cigarette industries.

I completely understand the concerns about the high rate of use of electronic cigarettes by young people in Canada, and I agree that action should be taken to reduce this. However, I am writing to you today because I do not believe the specific action being proposed, reducing the maximum permissible concentration of nicotine in e-cig liquids to 20 mg/ml, will have the desired effects. In fact, it is my opinion that this rule will be more likely to cause greater harms to young people who use electronic cigarettes by causing them to inhale more aerosol (and hence toxicants) in order to obtain the desired pharmacological effects of nicotine. I also believe that the proposed rule will cause an overall harm to public health in Canada by inhibiting the potential for adult smokers to quit smoking and reduce their toxicant exposure by switching to electronic cigarettes.

My research team was among the first to demonstrate that modern pod-based electronic cigarettes containing a high concentration of nicotine in the liquid (approx. 59 mg/ml), when puffed on intensively (30 puffs in 10 minutes), are capable of rapidly delivering a high concentration of nicotine to the blood, comparable with a cigarette (2). This made us concerned that such devices may be highly addictive. However, while there is no doubt that such device/liquid combinations can be addictive, the scientific evidence to date is surprisingly consistent in showing that electronic cigarettes, including those with high nicotine liquids, are less addictive than cigarettes (e.g. 1, 3, 4). We have also published studies showing that the addiction level even among daily exclusive e-cig users who were previously smokers (generally those who are most addicted) remains low over years of use (5). We recently published a study that similarly found that users of high nicotine concentration salt-nicotine pod devices like Juul (who are typically young people) also show lower levels of addiction than

cigarette smokers (6). It is not entirely clear why this is the case, but in that paper we proposed a possible explanation as follows:

“One potential explanation for the relatively low dependence levels among users of efficient nicotine delivery devices could relate to the way that e-cigs including JUUL are used differently than cigarettes. Cigarettes are typically smoked in a concentrated burst of 5-15 puffs in approximately 4-10 min (R I Herning et al., 1981; Ronald I Herning et al., 1983; Strasser et al., 2004), leading to a fairly consistent and strong increase in blood nicotine levels (boost typically 10-30 ng/ml) (Hajek et al., 2020; M. A. Russell et al., 1976; Williams et al., 2010; Yingst et al., 2019). However, with ecigs, there is not a need to take several puffs in a short period of time, because the device will not burn out. Because of this, e-cig users learn to take puffs intermittently but less frequently over much longer periods (Baweja et al., 2016; Cooper et al., 2016; Yingst et al., 2019a), avoiding the high peaks and troughs in blood nicotine levels that characterize cigarette smoking. It is possible that this different pattern of nicotine absorption with e-cigs leads to lower levels of perceived dependence even with a device capable of delivering nicotine like a cigarette if used like a cigarette.”

The main point here is that the amount of nicotine absorbed from an electronic cigarette is not solely (or even mainly) determined by the concentration in the liquid. It is very much influenced by the design of the device (particularly the electrical power applied to the heating coil in the device, in watts), and it is very highly influenced by the individual user behavior (7).

Therefore, if the primary aim of this proposed rule is to limit the nicotine absorption and addiction among young people who use electronic cigarettes, it will very likely fail to do so. Those young people will easily change their behavior, to either take more frequent and larger puffs to get the desired nicotine level and effects, or by switching to more powerful devices that can deliver high blood nicotine concentrations (like a cigarette) with relatively low e-cig liquid nicotine concentrations (e.g. 4 mg/ml) (8). The main problem with either of these consequences is that the first results in inhalation of more aerosol (hence toxicants) and the second results in the liquid being exposed to higher coil temperatures, producing greater chemical reaction and also greater exposure to toxicants (7). This will worsen, not improve, the health of Canadian youth, without actually lowering their nicotine absorption at all.

With regards to the effects of liquid nicotine concentration on toxicant exposure and quitting among adult smokers, my colleagues and I recently completed a clinical trial that is highly relevant to this question (9). The first paper from this study is currently accepted for publication but not yet in the public domain. I urge you and your team to consider the results of this trial when they are published as I believe they are relevant to the question of the effects of high versus lower nicotine concentration in e-cig liquids on adult smoker behavior and toxicant exposure.

I share your concern regarding the complex problem of increasing youth e-cig use. Unfortunately the solution that is currently being proposed is simple and wrong. Health Canada has an excellent track record in the field of tobacco control, as indicated by the reduction in youth and adult cigarette smoking. I believe that some of the strategies that have been successful with youth cigarette smoking can also be successfully applied to e-cigs (e.g. mass media education campaigns). Better enforcement of existing laws with larger penalties for those selling to under-age youth may also help reduce youth access.

- (1) Foulds J, Veldheer S, Yingst J, Hrabovsky S, Wilson SJ, et al. Development of a questionnaire for assessing dependence on electronic cigarettes among a large sample of ex-smoking E-cigarette users. *Nicotine Tob Res.* 2015 Feb;17(2):186-92. PubMed PMID: 25332459
- (2) Yingst JM, Hrabovsky S, Hobkirk AL, Trushin N, Richie JP, Foulds J. Nicotine absorption profile among regular users of a pod-based electronic nicotine delivery system. *JAMA Open.* 2019 Nov 1;2(11):e1915494. doi: 10.1001/jamanetworkopen.2019.15494. PMID:31730180
- (3) Liu G, Wasserman E, Kong L, Foulds J. A comparison of nicotine dependence among exclusive E-cigarette and cigarette users in the PATH study. *Prev Med.* 2017 Nov;104:86-91. PubMed PMID: 28389330; NIHMSID: NIHMS868366; PubMed Central PMCID: PMC5868349.
- (4) Hammond D, Reid JL, Rynard VL, O'Connor RJ, Goniewicz ML, Piper ME, Bansal-Travers M. Indicators of dependence and attempts to quit vaping and smoking among youth in Canada, England and the USA. *Tobacco Control.* Online Feb 1:tobaccocontrol-2020-056269. doi: 10.1136/tobaccocontrol-2020-056269. Online ahead of print. PMID: 33526441
- (5) Du P, Fan T, Yingst J, Veldheer S, Hrabovsky S, Chen C, Foulds J. Changes in e-cigarette-use behaviors and dependence in long-term e-cigarette users. *Am J Preventive Med.* 2019 Sep;57(3):374-383. PMID: 31375364
- (6) Yingst J, Foulds J, Hobkirk A. Dependence and use characteristics of adult Juul electronic cigarette users. *Substance Use & Misuse.* 2021;56(1):61-66. doi: 10.1080/10826084.2020.1834582. Epub 2020 Oct 29. PMID: 33118854
- (7) Talih S, Salman R, El-Hage R, Karam E, Karaoghlanian N, El-Hellani A, Saliba N, Eissenberg T, Shihadeh A. Might limiting liquid nicotine concentration result in more toxic electronic cigarette aerosols? *Tob Control.* 2020 Jun 10: Online ahead of print. PMID: 32522818
- (8) Wagener TL, Floyd EL, Stepanov I, et al. Have combustible cigarettes Met their match? the nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. *Tob Control* 2017; 26:e23-e28.
- (9) Lopez AA, Cobb CO, Yingst JM, Veldheer S, Hrabovsky S, Yen MS, Foulds J, Eissenberg T. A transdisciplinary model to inform randomized clinical trial methods for electronic cigarette evaluation. *BMC Public Health.* 2016 Mar 3;16(1):217. doi: 10.1186/s12889-016-2792-8. PMID:26941050

I hope that these comments are helpful and wish you all the best in your work to improve the health of Canadians.

Sincerely,



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