



July 16, 2018

Dockets Management Staff [HFA-305]  
 Food and Drug Administration  
 5630 Fishers Lane, Room 1061  
 Rockville, MD 20852

Re: Docket No. FDA-2017-N-6189, Tobacco Product Standard for Nicotine Level of Combusted Cigarettes

The undersigned organizations submit these comments in the above-designated docket regarding the FDA’s Advance Notice of Proposed Rulemaking on a Tobacco Product Standard for Nicotine Level of Combusted Cigarettes.

**Introduction**

For decades, researchers have agreed that nicotine is the fundamental addictive agent in tobacco, leading the U.S. Surgeon General to affirmatively conclude in the 1988 report, *The Health Consequences of Smoking: Nicotine Addiction*, that, “nicotine is the drug in tobacco that causes addiction.”<sup>1</sup> Now, strong scientific evidence also demonstrates that reducing the nicotine

<sup>1</sup> U.S. Department of Health and Human Services (HHS). *The Health Consequences of Smoking: Nicotine Addiction. A Report of the Surgeon General*. 1988.

content to a very low level can reduce smoking and nicotine addiction.<sup>2</sup> Reducing nicotine levels in combustible tobacco products provides enormous potential to accelerate progress in preventing and reducing smoking and the death and disease it causes. We urge you to move forward with this proposal as quickly as possible.

As FDA noted in the Advance Notice of Proposed Rulemaking (ANPRM at 11822), reducing the nicotine content of cigarettes will: “(1) Give addicted users of cigarettes the choice and ability to quit more easily by reducing the nicotine to a minimally addictive or nonaddictive level and (2) reduce the risk of progression to regular use and nicotine dependence for persons who experiment with the tobacco products covered by the standard.” Making cigarettes minimally or non-addictive will prevent most kids from ever becoming regular smokers and will increase the number of smokers who make a quit attempt and successfully quit. The FDA estimates that this proposal would prevent more than 33 million youth and young adults from becoming regular smokers this century, prompt 5 million smokers to quit within one year (rising to 13 million in five years) and save more than 8 million lives by the end of the century.<sup>3</sup> The impact of this policy would be historic. There are few actions FDA could take that would prevent as many young people from smoking and save as many lives.

It is important, however, that FDA consider a nicotine product standard as part of a comprehensive set of regulatory policies to curb the use of combustible tobacco products. Thus, moving toward adoption of such a standard would not obviate the need to implement, as soon as possible, proposals that include prohibiting menthol in cigarettes and characterizing flavors in all tobacco products, as well as graphic health warnings for cigarettes. Moreover, there is, and will continue to be, a need for FDA to exercise its full authority to reduce the use of and pursue public education campaigns directed at informing the public of the health risks of all tobacco products, including those subject to the nicotine reduction proposal. Reducing nicotine in combustible products to minimally or non-addictive levels will not make those products “safe,” and the public, particularly young people, need to understand that any use of these products will continue to carry substantial health risks.

## **I. Public Health Impact of Reducing Nicotine in Combustible Tobacco Products**

Despite great progress in curbing smoking prevalence in recent years, tobacco use – primarily smoking – remains the leading cause of preventable death and disease in the United States, killing more than 480,000 Americans every year.<sup>4</sup> Nearly 38 million Americans currently

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<sup>2</sup> World Health Organization (WHO) Study Group on Tobacco Product Regulation, *Global Nicotine Reduction Strategy*, 2015, [http://apps.who.int/iris/bitstream/10665/189651/1/9789241509329\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/189651/1/9789241509329_eng.pdf?ua=1).

<sup>3</sup> Apelberg, BJ, et al., “Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States,” *New England Journal of Medicine*, published online March 15, 2018. See also Tobacco Product Standard for Nicotine Level of Combusted Cigarettes; Advanced Notice of Proposed Rulemaking, 83 Fed. Reg. at 11818 (March 16, 2018).

<sup>4</sup> HHS, *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*, 2014.

smoke and every day about 2,300 kids try their first cigarette and another 350 additional kids become regular smokers.<sup>5</sup> Approximately half of continuing smokers will die prematurely as a result of their addiction, losing at least a decade of life on average compared to nonsmokers.<sup>6</sup>

Reducing the nicotine content in cigarettes to minimally or non-addictive levels will prevent young people who experiment from becoming addicted and save them from a lifetime of addiction, tobacco-caused disease, and premature death. It also will reduce the level of nicotine dependence in adult smokers, making it easier for them to quit. Ultimately, this will dramatically reduce the number of adult smokers. The FDA estimates that reducing nicotine levels in combusted tobacco products would prevent more than 33 million youth and young adults from initiating regular smoking by 2100. In addition, within five years, the FDA estimates it would cause 13 million smokers to quit, including five million within just the first year of implementation. Ultimately, more than 8 million lives would be saved by the end of the century.<sup>7</sup>

#### **A. Reducing the Nicotine Content of Cigarettes will Help Smokers Quit**

As stated by a Philip Morris researcher in 1972, “*No one has ever become a cigarette smoker by smoking cigarettes without nicotine.*”<sup>8</sup> Nicotine is the primary addictive agent in cigarettes.<sup>9</sup> According to the U.S. Surgeon General, “the addiction caused by the nicotine in tobacco smoke is critical in the transition of smokers from experimentation to sustained smoking and, subsequently, in the maintenance of smoking for the majority of smokers who want to quit.”<sup>10</sup> Most adult smokers want to quit (nearly 70 percent) and wish they had never started (about 90 percent), but overcoming an addiction to nicotine is difficult and smokers often need to make multiple quit attempts before succeeding.<sup>11</sup>

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<sup>5</sup> CDC, “Current Cigarette Smoking Among Adults – United States, 2016,” *Morbidity and Mortality Weekly Report (MMWR)* 67(2):53-59, January 19, 2018. <https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6702a1-H.pdf>. Substance Abuse and Mental Health Services Administration (SAMHSA), HHS, *Results from the 2016 National Survey on Drug Use and Health, NSDUH: Detailed Tables*, 2017. <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

<sup>6</sup> HHS, *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*, 2014.

<sup>7</sup> Apelberg, BJ, et al., “Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States,” *New England Journal of Medicine*, published online March 15, 2018. See also Tobacco Product Standard for Nicotine Level of Combusted Cigarettes; Advanced Notice of Proposed Rulemaking, 83 Fed. Reg. at 11818 (March 16, 2018).

<sup>8</sup> Philip Morris, Dunn, W Jr., “Motives And Incentives In Cigarette Smoking”; R107. 1972. <https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/jspf0085>. For additional industry quotes on nicotine, see Campaign for Tobacco-Free Kids fact sheet, “Tobacco Company Quotes: Nicotine as a Drug,” <https://www.tobaccofreekids.org/research/factsheets/pdf/0009.pdf>.

<sup>9</sup> HHS, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*, 2010.

<sup>10</sup> HHS, *The Health Consequences of Smoking—50 Years of Progress, A Report of the Surgeon General*, 2014. See also, HHS, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General*, 2010, <http://www.ncbi.nlm.nih.gov/books/NBK53017/>.

<sup>11</sup> Babb, S, et al., “Quitting Smoking Among Adults—United States, 2000—2015,” *MMWR* 65:1457–1464, 2017. Fong, G., et al., “The Near-Universal Experience of Regret Among Smokers in Four Countries: Findings from

Research demonstrates that significantly reducing nicotine levels holds great promise for accelerating progress in reducing smoking. Scientific evidence establishes that it is possible to lower nicotine levels in ways that dramatically reduce dependence. Based on a comprehensive review of the evidence, the World Health Organization Study Group on Tobacco Product Regulation concluded that reducing nicotine content in cigarettes could:<sup>12</sup>

- Reduce smoking acquisition and progression to addiction;
- Increase cessation and reduce relapse; and, ultimately,
- Reduce smoking prevalence.

The first large scale clinical trial of very low nicotine content (VLNC) cigarettes in the US, conducted in 2013-2014, randomly assigned over 800 smokers to use their usual brand of cigarettes or cigarettes with varying levels of nicotine for six weeks. Smokers assigned to smoke cigarettes with lower nicotine content smoked fewer cigarettes, reduced their exposure and dependence to nicotine, and reduced cravings, compared to the control group. The same study also found that those smoking cigarettes with the lowest nicotine content (0.4 mg/g) were twice as likely to report trying to quit in the 30 days after the study ended compared to those smoking cigarettes with 15.8 mg/g (34% vs. 17%). Smokers assigned to smoke cigarettes with 2.4 mg/g nicotine or less smoked between 23 and 30 percent fewer cigarettes per day at six-week follow-up compared to smokers assigned to smoke cigarettes with 15.8 mg/g nicotine.<sup>13</sup>

Other smaller studies have shown that use of reduced nicotine cigarettes leads to reductions in smoking, nicotine dependence, and biomarkers of exposure to nicotine and other toxins.<sup>14</sup> Research also shows that reduced nicotine cigarettes increase abstinence among smokers trying to quit.<sup>15</sup> For example, a 2009-2010 randomized controlled trial in New Zealand assigned over 1400 smokers seeking treatment from the Quitline to receive VLNC cigarettes with standard Quitline care (nicotine replacement therapy and behavioral counseling) for six

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the International Tobacco Control Policy Evaluation Survey,” *Nicotine & Tobacco Research*, Vol. 6, Supplement 3, December 2004.

<sup>12</sup> WHO, *Global Nicotine Reduction Strategy*, 2015.

<sup>13</sup> Donny, EC, et al., “Randomized trial of reduced-nicotine standards for cigarettes,” *New England Journal of Medicine*, 373: 1340-1349, 2015.

<sup>14</sup> See e.g., Donny EC, et al. Smoking in the absence of nicotine: behavioral, subjective and physiological effects over 11 days. *Addiction* 2007; 102: 324-34. Benowitz NL, et al., Nicotine and carcinogen exposure with smoking of progressively reduced nicotine content cigarette. *Cancer Epidemiol Biomarkers Prev* 2007; 16: 2479-85. Benowitz NL, et al., Urine nicotine metabolite concentrations in relation to plasma cotinine during low-level nicotine exposure. *Nicotine & Tobacco Research* 2009; 11: 954-60. Benowitz NL, et al. Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes. *Cancer Epidemiol Biomarkers Prev* 2012; 21: 761-9. Hatsukami DK, et al. Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation. *Addiction* 2010; 105: 343-55.

<sup>15</sup> See e.g., Walker, N, et al., “The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial,” *Addiction*, 107(10): 1857-1867, 2012. McRobbie, H, et al., “Complementing the standard multicomponent treatment for smokers with denicotinized cigarettes: a randomized controlled trial,” *Nicotine & Tobacco Research*, 18(5): 1134-1141, 2016.

weeks, or Quitline care alone. At 6-month follow-up, smokers who had received VLNC cigarettes were more likely to have quit smoking (33% vs. 28% seven-day point prevalence abstinence; 23% vs. 15% continuous abstinence).<sup>16</sup> This evidence suggests that VLNC cigarettes can help smokers who are making a quit attempt.

## **B. Reducing the Nicotine Content of Combustibles Will Prevent Kids from Becoming Addicted Smokers**

The FDA noted in the ANPRM (at 11821, 11823-11824) the powerful addictiveness of nicotine, particularly on the adolescent brain. Tobacco use almost always begins during adolescence and adolescents are particularly vulnerable to the addictive effects of nicotine because the brain continues to develop until about age 25. Because adolescence and young adulthood are critical periods of growth and development, exposure to nicotine may have lasting, adverse consequences on brain development.<sup>17</sup> The parts of the brain most responsible for decision making, impulse control, sensation seeking, and susceptibility to peer pressure continue to develop and change through young adulthood.<sup>18</sup> As a result, nicotine exposure during adolescence may result in impaired attention and memory, problems with learning, reduced self-control and anxiety.<sup>19</sup> Nicotine not only harms the adolescent brain, but is critical to the progression to regular smoking behavior, reinforcing a behavior that exposes smokers to the harmful chemicals responsible for tobacco-related death and disease. While ethical considerations limit the possibilities for research of VLNC on adolescents, a secondary analysis of data from the randomized controlled trial described earlier (Donny et al., 2015), found that young adults smoked fewer VLNC cigarettes per day than older adults after two weeks in the trial, suggesting that younger populations may be more sensitive and responsive to a nicotine reduction policy.<sup>20</sup>

## **C. Vulnerable Populations Will Benefit from a Nicotine Reduction Policy**

As smoking rates have declined nationally, smoking has become increasingly concentrated among certain vulnerable populations. According to data from the 2012-2014

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<sup>16</sup> Walker, N, et al., “The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial,” *Addiction*, 107(10): 1857-1867, 2012.

<sup>17</sup> HHS. *The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General*, 2014; Institute of Medicine, *Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products*, Washington, DC: The National Academies Press, 2015.

<sup>18</sup> Institute of Medicine, *Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products*, Washington, DC: The National Academies Press, 2015.

<sup>19</sup> England, LJ, et al., “Nicotine and the Developing Human: A Neglected Element in the Electronic Cigarette Debate.” *American Journal of Preventive Medicine*, 2015; Goriounova NA, Mansvelder HD, “Short-and Long-Term Consequences of Nicotine Exposure During Adolescence for Prefrontal Cortex Neuronal Network Function,” *Cold Spring Harbor Perspectives in Medicine*, 2012; Steinberg, Laurence, “Should the Science of Adolescent Brain Development Inform Public Policy?,” *Issues in Science and Technology*, Volume XXVIII, Issue 3, Spring 2012.

<sup>20</sup> Cassidy, RN, et al., “Age moderates smokers’ subjective response to very low nicotine content cigarettes: evidence from a randomized controlled trial,” *Nicotine & Tobacco Research*, published online April 28, 2018.

National Survey on Drug Use and Health (NSDUH), 33.3% of adults with any mental illness were current (past month) smokers, compared to 20.7% of adults without any mental illness.<sup>21</sup> Further, about three out of ten smokers (29.5%) have a mental illness.<sup>22</sup> Additional national data from the National Health Information Survey (NHIS) of adults ages 18 and over find that 35.8 percent of adults with serious psychological distress are current smokers, compared to 14.7 percent of adults without serious psychological distress.<sup>23</sup>

It is important to ensure that a nicotine reduction policy would not exacerbate existing disparities by causing negative side effects for those with affective disorders. Fortunately, the evidence to date indicates that these populations do in fact benefit from VLNC cigarettes. A secondary analysis of data from the randomized controlled trial described earlier (Donny et al., 2015) found that smokers with elevated depressive symptoms at baseline who were assigned to smoke VLNC cigarettes did in fact show lower smoking rates and nicotine dependence, without worsening depressive symptoms.<sup>24</sup> Preliminary *ad libitum* smoking session studies have also found that VLNC cigarettes do not affect psychiatric symptoms in schizophrenic patients and result in a reduction in cigarette craving, total puff volume, and nicotine withdrawal symptoms.<sup>25</sup> VLNC cigarettes also have reduced addiction potential in other vulnerable populations, including smokers with opioid dependence and socioeconomically disadvantaged women, without substantial impact on withdrawal, craving, or compensatory smoking.<sup>26</sup>

## **II. A Nicotine Content Standard Should Apply to Other Combustible Tobacco Products (ANPRM Section A, Scope, Question 1)**

To realize the potential public health benefits of a nicotine product standard, FDA must extend that standard beyond cigarettes, to other combustible tobacco products, particularly those that serve as or might serve as substitutes for cigarettes, such as roll-your-own tobacco (RYO)

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<sup>21</sup> Lipari, R.N. and Van Horn, S.L. “Smoking and mental illness among adults in the United States.” *The CBHSQ Report*: March 30, 2017. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD, [https://www.samhsa.gov/data/sites/default/files/report\\_2738/ShortReport-2738.html](https://www.samhsa.gov/data/sites/default/files/report_2738/ShortReport-2738.html).

<sup>22</sup> CDC, “Vital Signs: Current Cigarette Smoking Among Adults Aged ≥18 Years with Mental Illness—United States, 2009-2011,” *MMWR*, 62(5): 81-87, 2013. NSDUH defines any mental illness as “having a mental, behavioral, or emotional disorder, excluding developmental and substance use disorders, in the past 12 months” and defines current smoking as “smoking all or part of a cigarette within the 30 days preceding the interview.”

<sup>23</sup> CDC, “Current Cigarette Smoking Among Adults – United States, 2016,” *MMWR* 67(2):53-59, January 19, 2018. Serious psychological distress defined by the Kessler psychological distress scale. Across all age groups, current cigarette smoking increased significantly for each of the four categories of psychological distress (no, low, moderate, high).

<sup>24</sup> Tidey, JW, et al., “Effects of 6-week use of reduced-nicotine content cigarettes in smokers with and without elevated depressive symptoms,” *Nicotine & Tobacco Research*, 19(1): 59-67, 2017.

<sup>25</sup> Tidey, JW, et al., “Smoking topography characteristics of very low nicotine content cigarettes, with and without nicotine replacement, in smokers with schizophrenia and controls,” *Nicotine & Tobacco Research*, 18(9): 1807-1812, 2016. Tidey, JW, et al., “Separate and combined effects of very low nicotine cigarettes and nicotine replacement in smokers with schizophrenia and controls,” *Nicotine & Tobacco Research*, 15(1): 121-129, 2013.

<sup>26</sup> Higgins, ST, et al., “Addiction potential of cigarettes with reduced nicotine in populations with psychiatric disorders and other vulnerabilities to tobacco addiction,” *JAMA Psychiatry*, 74(1): 1056-1064, 2017

and smaller cigars. As FDA noted in the ANPRM (at 11825), other combusted tobacco products have similar negative health effects to cigarettes and cigarette smokers may switch to these products if the nicotine reduction standard is only applied to cigarettes. Extending the proposed nicotine reduction policy to other combustible tobacco products will limit the possibility that cigarette smokers will switch to other dangerous combustible products. Furthermore, extending the nicotine standard to these products, which are often flavored and popular among youth, will prevent youth experimenters from becoming addicted to these and other tobacco products. It will also prevent tobacco manufacturers from circumventing a nicotine content standard in cigarettes by marketing and developing non-cigarette substitutes like the small flavored cigars the industry introduced after flavored cigarettes were removed from the market.

### **A. The Tobacco Industry Manipulates Loopholes in Product Regulation**

History shows that the tobacco industry is adept in manipulating loopholes in tobacco control regulations. Tobacco companies have skillfully modified their products to circumvent regulation and minimize the effectiveness of policies designed to reduce tobacco use. For example, in the 1960s and 1970s, “little cigars” that look like cigarettes were developed to avoid the ban on broadcast advertising of cigarettes and higher cigarette taxes.<sup>27</sup>

More recently, manufacturers have modified their products to be classified as cigars rather than cigarettes to evade the TCA’s prohibition of characterizing flavors in cigarettes<sup>28</sup> and the use of misleading cigarette descriptors such as “light” and “low.”<sup>29</sup> The 2012 Surgeon General’s report, *Preventing Tobacco Use Among Youth and Young Adults*, noted that flavored cigarettes such as Sweet Dreams re-emerged as Sweet Dreams flavored cigars after the federal restriction on flavored cigarettes went into effect.<sup>30</sup> In October 2009, U.S. Representatives Henry Waxman and Bart Stupak sent letters to two flavored cigarette companies, Cheyenne International and Kretek International, that began making little cigars shortly after the federal flavored cigarette ban went into effect.<sup>31</sup> Rep. Waxman discovered that Kretek International

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<sup>27</sup> Delnevo, CD & Hrywna, M, “A Whole ‘Nother Smoke’ or a Cigarette in Disguise: How RJ Reynolds Reframed the Image of Little Cigars,” *American Journal of Public Health* 97(8):1368-75, August 2007.

<sup>28</sup> Delnevo, CD, et al., “Close, but no cigar: certain cigars are pseudo-cigarettes designed to evade regulation,” *Tobacco Control* 26(3):349-354, May 2017. Delnevo, CD & Hrywna, M, “Clove cigar sales following the US flavoured cigarette ban,” *Tobacco Control* 24(e4):e246-50, December 2015.

<sup>29</sup> See generally, Campaign for Tobacco-Free Kids, *Not Your Grandfather’s Cigar: A New Generation of Cheap and Sweet Cigars Threatens a New Generation of Kids*, March 13, 2013, at 14-15 (*Not Your Grandfather’s Cigar*),

[http://www.tobaccofreekids.org/content/what\\_we\\_do/industry\\_watch/cigar\\_report/2013CigarReport\\_Full.pdf](http://www.tobaccofreekids.org/content/what_we_do/industry_watch/cigar_report/2013CigarReport_Full.pdf).

<sup>30</sup> HHS, *Preventing Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012, <http://www.cdc.gov/Features/YouthTobaccoUse/>.

<sup>31</sup> House Committee on Energy & Commerce, “Energy and Commerce Committee Requests Information on Sales and Marketing of Flavored Tobacco Products,” October 2, 2009, accessed April 18, 2012 at <http://democrats.energycommerce.house.gov/index.php?q=news/energy-and-commerce-committee-requests-information-on-sales-and-marketing-of-flavored-tobacco-p>.

intentionally changed its cigarettes to cigars to exploit a loophole in the TCA.<sup>32</sup> In December 2016, the FDA issued warning letters to four tobacco manufacturers – Swisher International, Inc., Cheyenne International LLC, Prime Time International Co. and Southern Cross Tobacco Company Inc. – for marketing and selling fruit-flavored cigarettes labeled as cigars, in violation of the Tobacco Control Act.<sup>33</sup>

Tobacco companies have also added weight to filters to allow for reclassification of their cigarettes or “little cigars” as “large cigars” subject to lower federal excise taxes.<sup>34</sup> Moreover, tobacco companies intentionally designed and marketed little cigars as similar products to cigarettes to appeal to cigarette smokers.<sup>35</sup>

FDA recognized reclassification as a potential problem in its Final Regulatory Impact Analysis of the final deeming rule when it stated, “Deeming all tobacco products, except accessories of a newly deemed tobacco product, to be subject to chapter IX of the FD&C Act would be the necessary first step to rectify an institutional failure in which tobacco products that are close substitutes are not regulated by FDA in a like manner. ...Historically, when products have been taxed or regulated differently, substitutions have occurred.”<sup>36</sup>

There is little doubt that tobacco companies will promote cigars and potentially other combustible tobacco products as alternatives to cigarettes if the nicotine policy does not address other forms of combustible tobacco. Failure to extend the prohibition to other combusted tobacco products would greatly limit the chances for the regulation to accomplish its goal.

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<sup>32</sup> Representative Henry A. Waxman, “Rep. Waxman Urges FDA to Ban Clove-Flavored Cigars,” Letter to FDA Commissioner Margaret Hamburg, March 28, 2011, accessed April 18, 2012 at <http://democrats.energycommerce.house.gov/index.php?q=news/rep-waxman-urges-fda-to-ban-clove-flavored-cigars>.

<sup>33</sup> FDA, Center for Tobacco Products, “FDA takes action against four tobacco manufacturers for illegal sales of flavored cigarettes labeled as little cigars or cigars,” December 9, 2016, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm532563.htm>.

<sup>34</sup> Delnevo, CD, et al., “Close, but no cigar: certain cigars are pseudo-cigarettes designed to evade regulation,” *Tobacco Control* 26(3):349-354, May 2017. Campaign for Tobacco-Free Kids, *Not Your Grandfather’s Cigar: A New Generation of Cheap and Sweet Cigars Threatens a New Generation of Kids*, March 13, 2013, at 14-15 (*Not Your Grandfather’s Cigar*), [http://www.tobaccofreekids.org/content/what\\_we\\_do/industry\\_watch/cigar\\_report/2013CigarReport\\_Full.pdf](http://www.tobaccofreekids.org/content/what_we_do/industry_watch/cigar_report/2013CigarReport_Full.pdf) at 15.

<sup>35</sup> Delnevo, CD, et al., “Close, but no cigar: certain cigars are pseudo-cigarettes designed to evade regulation,” *Tobacco Control* 26(3):349-354, May 2017.

<sup>36</sup> FDA, *Deeming Tobacco Products to be Subject to the Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations Restricting the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Product Packages and Advertisements, Final Regulatory Impact Analysis; Final Regulatory Flexibility Analysis; Unfunded Mandates Reform Act Analysis*, May 2016, at 60-61, <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/UCM500254.pdf>.



## B. Cigars Are a Harmful and Addictive Substitute for Cigarettes

There is no rational basis for reducing nicotine levels in cigarettes, while leaving cigars highly addictive. Cigars pose an increased risk of disease and addiction. Cigar smoke contains many of the same harmful constituents as cigarette smoke and may have higher levels of several harmful compounds. Cigar smoking causes cancer of the oral cavity, larynx, esophagus and lung and some cigar smokers are at increased risk for heart disease, chronic obstructive pulmonary disease (COPD) and an aortic aneurysm.<sup>37</sup>

Furthermore, cigars contain nicotine and can deliver nicotine at levels high enough to produce dependence among cigar smokers.<sup>38</sup> Nicotine content is not always associated with the size of the cigar. A study found that some cigarillos had higher levels of free nicotine per mass compared to large cigars, leading the authors to state, “consumers smoking the same brand of cigar may unintentionally be exposed to varying doses of nicotine and potentially other smoke constituents.”<sup>39</sup>

Nicotine levels in cigars vary by product and the type of tobacco used. One full-size cigar may contain as much tobacco as a whole pack of cigarettes and thus contains much more nicotine than one cigarette. Cigarettes contain an average of about 10-15 mg of nicotine;<sup>40</sup> many popular brands of larger cigars contain between 100 and 200 mg.<sup>41</sup>

The amount of nicotine delivered to the cigar smoker depends on various factors, such as how the cigar is smoked, the number of puffs taken, and the degree of inhalation.<sup>42</sup> The high pH of cigar smoke means that the nicotine is in its free, unprotonated form, making it easily

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<sup>37</sup> National Cancer Institute (NCI), *Cigars: Health Effects and Trends. Smoking and Tobacco Control Monograph No. 9*, 1998, [http://cancercontrol.cancer.gov/Brp/tcrb/monographs/9/m9\\_complete.pdf](http://cancercontrol.cancer.gov/Brp/tcrb/monographs/9/m9_complete.pdf).

<sup>38</sup> Henningfield, JE, et al., “Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States,” *Nicotine & Tobacco Research* 1(2):163-168, 1999, at 166. NCI Monograph 9, at 186, 191. Baker, F, et al., “Health Risks Associated With Cigar Smoking,” *Journal of the American Medical Association* 284(6):735-740, 2000, at 737. Fabian, LA, et al., “Ad lib Smoking of Black & Mild Cigarillos and Cigarettes,” *Nicotine & Tobacco Research* 14(3):368-371, March 2012, at 370. Goel, R, et al., “A Survey of Nicotine Yields in Small Cigar Smoke: Influence of Cigar Design and Smoking Regimens,” *Nicotine & Tobacco Research*, published online September 15, 2017. Pickworth, WB, et al., “Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure,” *Tobacco Regulatory Science* 3(Suppl 1):S72-S83, April 2017, at S79. Claus, ED, “Use Behaviors, Dependence, and Nicotine Exposure Associated with Ad Libitum Cigar Smoking,” *Tobacco Regulatory Science* 4(1):548-561, 2018, at 558.

<sup>39</sup> Koszowski, B, et al., “Nicotine Content and Physical Properties of Large Cigars and Cigarillos in the United States,” *Nicotine & Tobacco Research* 20(3):393-398, 2018, at 395, 397.

<sup>39</sup> American Cancer Society, “Is Any Type of Smoking Safe?” March 6, 2018, <https://www.cancer.org/cancer/cancer-causes/tobacco-and-cancer/is-any-type-of-smoking-safe.html>.

<sup>40</sup> Benowitz, N and Henningfield, J., “Reducing the nicotine content to make cigarettes less addictive,” *Tobacco Control*, 22:i14-i17, 2013.

<sup>41</sup> American Cancer Society, “Is Any Type of Smoking Safe?” March 6, 2018, <https://www.cancer.org/cancer/cancer-causes/tobacco-and-cancer/is-any-type-of-smoking-safe.html>.

<sup>42</sup> Henningfield, JE, et al., “Nicotine concentration, smoke pH and whole tobacco aqueous pH of some cigar brands and types popular in the United States,” *Nicotine & Tobacco Research* 1(2):163-168, 1999, at 165. NCI Monograph 9, at 186.

absorbed through the oral mucosa, even if the users do not fully inhale the smoke.<sup>43</sup> A leading review of the science of cigar smoking concluded that, “[c]igars are capable of providing high levels of nicotine at a sufficiently rapid rate to produce clear physiological and psychological effects that lead to dependence, even if the smoke is not inhaled.”<sup>44</sup>

Authors of a recent study looking at a variety of cigar products noted, “it is clear that all cigar products delivered significant and addictive quantities of nicotine and CO – findings that support the rationale for their regulation.”<sup>45</sup>

Exempting cigars from a reduced nicotine standard is likely to lead current cigarette smokers to switch to cigars or use both cigarettes and cigars to satisfy their need for nicotine. It is not uncommon for cigarette smokers to replace cigarettes with cigars.<sup>46</sup> According to 2013-2014 data from the Population Assessment of Tobacco and Health (PATH) study, nearly 30 percent of premium cigars smokers were former cigarette smokers, as were 10 to 15 percent of non-premium cigar users (non-premium large cigars, cigarillos, filtered cigars).<sup>47</sup> The 2012-2013 National Adult Tobacco Survey (NATS) found similar results - 23 percent of premium cigar smokers, 15.3 percent of cigarillo/mass market cigar smokers, and 12.3 percent of little filtered cigar smokers were former cigarette smokers.<sup>48</sup>

Secondary cigar smokers, those who smoked cigarettes before smoking cigars, often inhale and smoke more than cigar smokers who have never used cigarettes (primary cigar smokers).<sup>49</sup> Because of their tendency to inhale the smoke, secondary cigar smokers can take in

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<sup>43</sup> NCI Monograph 9, at ii, 4, 11, 97, 183, 191.

<sup>44</sup> Baker, F., et al., “Health Risks Associated With Cigar Smoking,” *Journal of the American Medical Association*, 284(6): 735-740, 2000, at 737.

<sup>45</sup> Pickworth, WB, et al., “Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure,” *Tobacco Regulatory Science* 3(Suppl 1):S72-S83, April 2017, at S79.

<sup>46</sup> Corey, CG, et al., “U.S. adult cigar smoking patterns, purchasing behaviors, and reasons for use according to cigar type: Findings from the Population Assessment of Tobacco and Health (PATH) Study, 2013-14,” *Nicotine & Tobacco Research*, published online September 15, 2017. Cohn, A, et al., “The Other Combustible Products: Prevalence and Correlates of Little Cigar/Cigarillo Use Among Cigarette Smokers,” *Nicotine & Tobacco Research* 17(12):1473-1481, 2015.

<sup>47</sup> Corey, CG, et al., “U.S. adult cigar smoking patterns, purchasing behaviors, and reasons for use according to cigar type: Findings from the Population Assessment of Tobacco and Health (PATH) Study, 2013-14,” *Nicotine & Tobacco Research*, published online September 15, 2017.

<sup>48</sup> Corey, CG, et al., “Little Filtered Cigar, Cigarillo, and Premium Cigar Smoking Among Adults — United States, 2012-2013,” *MMWR* 63(30):650-654, August 1, 2014, at 652, 653. The study authors defined premium cigar smokers as “those reporting their usual cigar did not have a filter or tip and the name of their usual brand was a brand name of a hand-rolled cigar or a cigar described by the manufacturer or merchant as containing high-grade tobaccos in the filler, binder, or wrapper.”

<sup>49</sup> Claus, ED, “Use Behaviors, Dependence, and Nicotine Exposure Associated with Ad Libitum Cigar Smoking,” *Tobacco Regulatory Science* 4(1):548-561, 2018. Rosenberry, ZR, Pickworth, WB, & Koszowski, B, “Large Cigars: Smoking Topography and Toxicant Exposure,” *Nicotine & Tobacco Research* 20(2):183-191, 2018, at 189.

more nicotine compared to primary cigar smokers.<sup>50</sup> They also show higher scores of nicotine dependence than primary cigar smokers.<sup>51</sup>

PATH data from 2013-2014 show that a fair number of cigar smokers also smoke cigarettes (dual use): nearly 30 percent (29.9%) of premium cigar users and more than half of users of other cigar products (non-premium large cigars, cigarillos, filtered cigars) were also current cigarette smokers.<sup>52</sup> The 2012-2013 NATS reported similar results, with 35.1 percent of premium cigar smokers, 58.3 percent of cigarillo/mass market cigar smokers, and 75.2 percent of little filtered cigar smokers dual using with cigarettes.<sup>53</sup> Cigarette use in the past 30 days can predict current cigar use.<sup>54</sup>

Like secondary cigar smokers, dual users tend to inhale cigar smoke, compared to cigar smokers who never smoked cigarettes.<sup>55</sup> Dual users smoke cigars in such a way as to obtain a satisfactory level of nicotine,<sup>56</sup> but they also show greater levels of dependence than exclusive cigar users.<sup>57</sup> Adolescents who ever used cigars products (cigars, cigarillos, or little cigars) or used them in the past 30 days reported more frequent cigarette smoking in the past month, more daily smoking in the past month, and, notably, higher levels of nicotine dependence compared to adolescents who did not use cigar products.<sup>58</sup>

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<sup>50</sup> NCI Monograph 9, at 94.

<sup>51</sup> Claus, ED, "Use Behaviors, Dependence, and Nicotine Exposure Associated with Ad Libitum Cigar Smoking," *Tobacco Regulatory Science* 4(1):548-561, 2018.

<sup>52</sup> Corey, CG, et al., "U.S. adult cigar smoking patterns, purchasing behaviors, and reasons for use according to cigar type: Findings from the Population Assessment of Tobacco and Health (PATH) Study, 2013-14," *Nicotine & Tobacco Research*, published online September 15, 2017.

<sup>53</sup> Corey, CG, et al., "Little Filtered Cigar, Cigarillo, and Premium Cigar Smoking Among Adults — United States, 2012-2013," *MMWR* 63(30):650-654, August 1, 2014, at 652, 653. The study authors defined premium cigar smokers as "those reporting their usual cigar did not have a filter or tip and the name of their usual brand was a brand name of a hand-rolled cigar or a cigar described by the manufacturer or merchant as containing high-grade tobaccos in the filler, binder, or wrapper."

<sup>54</sup> Cullen, J, et al., "Seven-Year Patterns in US Cigar Use Epidemiology Among Young Adults Aged 18–25 Years: A Focus on Race/Ethnicity and Brand," *American Journal of Public Health* 101(10):1955-62, October 2011, at 1958-1959.

<sup>55</sup> Baker, F, et al., "Health Risks Associated With Cigar Smoking," *Journal of the American Medical Association* 284(6):735-740, 2000, at 737. NCI Monograph 9, at 185.

<sup>56</sup> Pickworth, WB, et al., "Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure," *Tobacco Regulatory Science* 3(Suppl 1):S72-S83, April 2017, at 7. Rosenberry, ZR, Pickworth, WB, & Koszowski, B, "Large Cigars: Smoking Topography and Toxicant Exposure," *Nicotine & Tobacco Research* 20(2):183-191, 2018, at 189.

<sup>57</sup> Rostron, BL, Schroeder, MJ, & Ambrose, BK, "Dependence symptoms and cessation intentions among US adult daily cigarette, cigar, and e-cigarette users, 2012-2013," *BMC Public Health* 16:814, 2016.

<sup>58</sup> Schuster, RM, Hertel, AW, & Mermelstein, R, "Cigar, Cigarillo, and Little Cigar Use Among Current Cigarette-Smoking Adolescents," *Nicotine & Tobacco Research* 15(5):925-931, May 2013, at 927-928.

**C. Hookah (Waterpipe) Tobacco is Harmful and Addictive (ANPRM Section A, Question 4)**

In a typical waterpipe session, smokers are subjected to up to more than twice the nicotine exposure as the smoker of a single cigarette.<sup>59</sup> Research shows that waterpipe tobacco use is associated with nicotine dependence, including experiences of withdrawal and difficulty quitting, at least among some users.<sup>60</sup> Given its addiction potential, waterpipe tobacco should not be excluded from a nicotine product standard.

Studies have shown that hookah smoke contains many of the toxins and carcinogens found in cigarettes.<sup>61</sup> Some of these harmful components are in gaseous form and others are particulates. At least 82 toxicants and carcinogens have been identified in waterpipe tobacco smoke, including tobacco-specific nitrosamines (TSNAs), polycyclic aromatic hydrocarbons (PAHs), and heavy metals.<sup>62</sup> In addition, the aerosol contains the toxins and carcinogens from the burning of the charcoal, including carbon monoxide. A recently published meta-analysis that analyzed 17 studies of waterpipe tobacco smoking found that a single waterpipe tobacco smoking session was associated with carbon monoxide exposure equivalent to more than half a pack of cigarettes and exposure to tar equivalent to more than two full packs of cigarettes.<sup>63</sup> None of these harmful components are eliminated by the passage of the smoke through the water and many of these harmful substances are delivered to the user's lungs.

According to the CDC, using a waterpipe to smoke tobacco poses serious health risks to smokers and others exposed to the smoke from the waterpipe tobacco.<sup>64</sup> Waterpipe tobacco use is linked to many of the same adverse health effects as cigarette smoking, such as lung, bladder and oral cancers and heart disease.<sup>65</sup> Other documented long-term effects include impaired

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<sup>59</sup> Primack B, et al. 2016. HHS, *Prevention Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012. Eissenberg, T and Shihadeh, A., 2009. Maziak, W, et al., "CO exposure, puff topography, and subjective effects in waterpipe tobacco smokers," *Nicotine & Tobacco Research*, 11(7): 806-811, 2006.

<sup>60</sup> Aboaziza, E and Eissenberg, T., "Waterpipe tobacco smoking: what is the evidence that it supports nicotine/tobacco dependence?" *Tobacco Control*, published online December 9, 2014.

<sup>61</sup> HHS, *Prevention Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012.

<sup>62</sup> Ward, KD, et al., "The waterpipe: an emerging epidemic in need of action," *Tobacco Control*, 24(S1): i1-i2, 2015. Sepetdijian, E, et al., "Measurement of 16 Polycyclic Aromatic Hydrocarbons in Narghile Waterpipe Tobacco Smoke," *Food and Chemical Toxicology*, 46: 1582-1590, 2008. Schubert, J., et al., "Mainstream Smoke of the Waterpipe: Does this Environmental Matrix Reveal as Significant Source of Toxic Compounds?" *Toxicology Letters*, 205(3): 279-284, 2011. Jacob, P., et al. "Nicotine, Carbon Monoxide and Carcinogen Exposure After a Single Use of a Water Pipe," *Cancer Epidemiology, Biomarkers, & Prevention*, 20: 2345-2353, 2011.

<sup>63</sup> Primack B, et al. Systematic review and meta-analysis of inhaled toxicants from waterpipe and cigarette smoking. *Public Health Reports* Jan. 2016. See also, HHS, *Prevention Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012. Eissenberg, T and Shihadeh, A. "Waterpipe tobacco and cigarette smoking: direct comparison of toxicant exposure," *American Journal of Preventive Medicine*, 37(6): 518-523, 2009. Maziak, W, et al., "CO exposure, puff topography, and subjective effects in waterpipe tobacco smokers," *Nicotine & Tobacco Research*, 11(7): 806-811.

<sup>64</sup> Centers for Disease Control and Prevention. "Hookahs." Available at [http://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/tobacco\\_industry/hookahs/](http://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/hookahs/). Accessed March 4, 2016.

<sup>65</sup> HHS, *Prevention Tobacco Use Among Youth and Young Adults, A Report of the Surgeon General*, 2012. Knishkowsky B, Amitai, Y. "Waterpipe (narghile) smoking: an emerging health risk behavior," *Pediatrics* 2005.

pulmonary function, chronic obstructive pulmonary disease, esophageal cancer and gastric cancer.<sup>66</sup> As a result of exposure to the dangerous chemicals in waterpipe tobacco smoke, research shows that even short-term waterpipe tobacco use is associated with acute health effects, including increased heart rate, blood pressure, reduced pulmonary function and carbon monoxide intoxication.<sup>67</sup> In a 2015 report, the World Health Organization Study group on tobacco product regulation surveyed the research to date and corroborated these findings.<sup>68</sup>

**D. The rule should prohibit other changes in cigarettes that might counteract the effect of the reduction in nicotine. (ANPRM Section B, Question 3)**

FDA notes that in addition to nicotine, other substances contained in cigarettes might also have the potential to produce dependence and be addictive and asks whether a proposed rule should establish maximum levels for such substances. It is important for FDA to establish a rule that prohibits any change in products subject to the rule that has the effect of diluting or offsetting the effect produced by the reduction in nicotine. Section 910 of the Tobacco Control Act prohibits tobacco product manufacturers from modifying tobacco products in the absence of a marketing order from FDA. Any product standard establishing a maximum level of nicotine in tobacco products should explicitly prohibit manufacturers from making other changes in a tobacco product with the effect of diluting or offsetting the reduction in dependence produced by reducing the nicotine content of such product.

**III. Implementation Considerations**

**A. Maximum Nicotine Level (ANPRM Section B, Question 1)**

When establishing a nicotine reduction level, FDA should seek a level that reduces the population harm caused by smoking. FDA should seek a level that prevents new users from developing dependence and stops the transition from experimental to regular use. The level should also reduce dependence among current users and make it easier for them to stop smoking. Because of variations in sensitivity to nicotine and the risk of dependence across individuals, to minimize the risk of dependence on a population-wide basis, FDA should set the maximum allowable nicotine at a level that produces the greatest reduction in dependence. To date, the research indicates that a nicotine content of 0.4 mg/g or less reduces dependence, taking into account the potential for individual differences in sensitivity to nicotine, and is technically feasible.<sup>69</sup> It is critical that there be no compromise in setting the nicotine level because a higher

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<sup>66</sup> El-Zaatari, ZM, et al., “Health effects associated with waterpipe smoking,” *Tobacco Control*, 24(S1): i31-i43, 2015.

<sup>67</sup> *Id.*

<sup>68</sup> World Health Organization, Study Group on Tobacco Product Regulation (“TobReg”), 2015.

<sup>69</sup> Donny, EC, et al., “Randomized trial of reduced-nicotine standards for cigarettes,” *New England Journal of Medicine*, 373: 1340-1349, 2015

nicotine level will not produce the benefits set forth by FDA and is not supported by the scientific evidence that underpins the FDA proposal.

**B. An Immediate Nicotine Content Reduction Will Have a Larger Public Health Impact than a Gradual Reduction (ANPRM Section C)**

Research shows that an immediate nicotine content reduction will have a greater public health benefit than a gradual reduction in nicotine content. A 20-week randomized controlled trial of 1200 adult smokers assigned smokers to normal nicotine content cigarettes, reduced nicotine content cigarettes (0.4 mg/g), or cigarettes with the nicotine content gradually reduced over the course of the study (from 15.8 mg/g to 0.4 mg/g). The smokers in the immediate nicotine reduction condition showed greater reduction in cigarettes per day, greater decreases in measures of dependence, higher rates and duration of abstinence, and greater reductions in biomarkers of smoke exposure.<sup>70</sup>

As the FDA noted in the ANPRM (at 11829), a stepped-down approach will likely facilitate more compensatory behavior by smokers. While VLNC cigarettes do not contain enough nicotine for compensation to be feasible, smokers may be able to compensate with intermediate-level nicotine cigarettes, smoking these products more intensely and exposing themselves to more toxicants.

Additionally, a stepped-down approach prolongs the implementation process and is more burdensome on farmers and manufacturers who will have to adjust to multiple nicotine content standards. Finally, this prolonged process increases the opportunities for consumers to stockpile cigarettes.

Given the stronger evidence for cessation for an immediate reduction approach and the greater implementation challenges of a stepped-down approach, it is clear that an immediate reduction in nicotine content is preferable.

**C. Reducing the Nicotine Content of Combustibles Will Not Lead to Compensation (ANPRM Section F, Question 4)**

One potential concern about reducing the nicotine level in cigarettes is that smokers may smoke more cigarettes or inhale smoke more deeply in order to obtain the nicotine fix they are accustomed to (“compensatory smoking”), which would have the unintended consequence of exposing them to even more harmful constituents. However, research to date shows that smokers in fact do not compensate in this manner when nicotine content is reduced to very low levels.<sup>71</sup>

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<sup>70</sup> Hatsukami, D. *Opening Session: Presidential Symposium Reducing Nicotine Content in Cigarettes: A Discussion of the Evidence and Policy Implications Panel Discussion*. Society for Research on Nicotine and Tobacco Annual Meeting, 2018.

<sup>71</sup> See e.g., Donny, EC, et al., “Randomized trial of reduced-nicotine standards for cigarettes,” *New England Journal of Medicine*, 373: 1340-1349, 2015. Hatsukami, DK, et al., “Compensatory smoking from gradual and

One study that examined the number of cigarettes smoked per day (CPD), carbon monoxide exposure and cotinine levels among smokers while they smoked reduced nicotine content cigarettes, found significant decreases in CPD and cotinine levels and a decrease (non-significant) in carbon monoxide exposure compared to when they smoked their usual brand, which suggests minimal, if any, compensatory smoking.<sup>72</sup> Similarly, a randomized clinical trial that compared outcomes from reduced nicotine cigarettes to standard nicotine cigarettes found that smokers of reduced nicotine cigarettes inhaled less smoke per cigarette, smoked fewer cigarettes and did not have a significant increase in the level of expired carbon monoxide, indicating that smokers did not compensate for the reduction in nicotine by increasing their smoking behavior.<sup>73</sup> Substantially reducing nicotine in the tobacco makes it almost impossible for smokers to compensate for the lower nicotine level by smoking more cigarettes, taking more puffs on the cigarette, or inhaling more deeply.

**D. FDA Must Counter Misperceptions about the Harms of Reduced Nicotine Products (ANPRM Section, B Question 4)**

Reducing the nicotine content of tobacco products will not render them harmless; in fact, products with lower nicotine levels will remain harmful and deadly. While nicotine is the primary addictive agent in cigarettes and is not benign, the overwhelming health consequences of smoking come from the more than 7,000 chemicals and 69 cancer-causing agents produced from combusted cigarettes.<sup>74</sup>

Some studies of adult smokers have shown that they perceive lower nicotine cigarettes to be less harmful than average cigarettes, incorrectly linking nicotine content with risk for smoking-related disease. For example, a 2015-2016 nationally representative survey found that nearly half (47.1%) of smokers thought that smoking VLNC cigarettes would be less likely to cause cancer than smoking regular cigarettes.<sup>75</sup> 2015 data from the FDA's nationally representative Health Information National Trends Survey (HINTS) found that three-quarters of people either did not know the relationship between nicotine and cancer (24%) or incorrectly believe that nicotine causes cancer (49%). It also found that 30 percent of respondents thought

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immediate reduction in cigarette nicotine content," *Cancer Epidemiology, Biomarkers & Prevention*, 24: 472-476, 2015. Benowitz, NL, et al., "Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes," *Cancer Epidemiology, Biomarkers & Prevention*, 21: 761-769, 2012. Hatsukami, DK, et al., "Nicotine reduction revisited: science and future directions," *Tobacco Control*, 19: e1-10, 2010. Hatsukami, DK, et al., "Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation," *Addiction*, 105: 343-355, 2010.

<sup>72</sup> Hatsukami, DK, et al., "Compensatory smoking from gradual and immediate reduction in cigarette nicotine content," *Cancer Epidemiology, Biomarkers & Prevention*, 24: 472-476, 2015.

<sup>73</sup> Donny, EC, et al., "Randomized trial of reduced-nicotine standards for cigarettes," *New England Journal of Medicine*, 373: 1340-1349, 2015.

<sup>74</sup> HHS, *The Health Consequences of Smoking—50 Years of Progress, A Report of the Surgeon General*, 2014, <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/>.

<sup>75</sup> Byron, JM, et al., "Public misperception that very low nicotine cigarettes are less carcinogenic," *Tobacco Control*, published online January 23, 2018.

that VLNC were less harmful than regular cigarettes.<sup>76</sup> In research trials, smokers assigned to use VLNC cigarettes also perceive them to be less harmful.<sup>77</sup>

It is critical for the FDA to carefully regulate the marketing of these products, and precede a nicotine reduction policy with public education campaigns to ensure adequate communication about the health risks of these products so as to not encourage non-smokers to experiment. Smokers should be encouraged to quit completely and be educated about the most effective ways to quit successfully.

While much of the public misunderstanding of the health effects of nicotine is to attribute undue health risk to nicotine, FDA also needs to be careful not to go too far in the other direction. While the most prominent concern about nicotine is its addictive impact, and approved nicotine replacement therapy (NRT) products have demonstrated that at low levels in carefully calibrated doses, nicotine is not the cause of serious disease, nicotine is not benign and the health impact of its long term use at higher levels is not well understood.

#### **IV. Technical Achievability**

##### **A. Reducing Nicotine in Cigarettes is Technologically Feasible (ANPRM Section E)**

Research demonstrates that reducing nicotine content in cigarettes to minimally or non-addictive levels is technologically feasible. Further, as noted in the ANPRM (at 11830-11832), there is a wide range of techniques available to reduce nicotine content. As FDA notes, more than 96 percent of nicotine can be successfully extracted while achieving a product that was “subjectively rated as average in smoking characteristics.”<sup>78</sup> Moreover, the FDA’s discussion in the ANPRM identifies several chemical extraction techniques that have been used successfully to reduce the nicotine level in cigarette tobacco (ANPRM, at 11831.)

Tobacco farmers and cigarette manufacturers can reduce the nicotine content of cigarette tobacco by using existing lower-nicotine tobacco plant varieties, creating new plant varieties through genetic manipulation, using tobacco leaves from certain parts of the plant that contain

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<sup>76</sup> O’Brien, EK, et al., “U.S. adults’ addiction and harm beliefs about nicotine and low nicotine cigarettes,” *Preventive Medicine*, 96: 94-100, 2017.

<sup>77</sup> Denlinger-Apte, RL, et al., “Low nicotine content descriptors reduce perceived health risks and positive cigarette ratings in participants using very low nicotine content cigarettes,” *Nicotine & Tobacco Research*, published online January 18, 2017. Pacek, LR, et al., “Perceived nicotine content of reduced nicotine content cigarettes is a correlate of perceived health risks,” *Tobacco Control*, published online July 22, 2017. 2017.

<sup>78</sup> 83 Fed. Reg. at 11826, citing Grubbs et al, “Process for Removal of Basic Materials,” Patent No. 5,018,540, May 28, 1991.



lower nicotine content, or using extraction technology to remove nicotine from tobacco during the manufacturing process.<sup>79</sup>

In fact, tobacco companies have already demonstrated their proficiency in reducing the nicotine level of cigarettes.<sup>80</sup> In the 1980s-1990s, Philip Morris produced three brands of low-nicotine cigarettes: Merit De-Nic, Benson & Hedges De-Nic and Next. Vector Tobacco introduced Quest, a low-nicotine cigarette, in 2003. The tobacco manufacturer, 22<sup>nd</sup> Century, currently produces Spectrum, a very low nicotine U.S.-grown tobacco cigarette, which is currently used in government-funded clinical research studies. Reducing nicotine content in cigarettes to minimally or non-addictive levels is also consistent with several tobacco companies' purported missions of shifting away from combustible tobacco products by "transforming tobacco" (R.J. Reynolds)<sup>81</sup> and investing in a "smoke-free future" (Philip Morris).<sup>82</sup>

The tobacco industry's own documents also show that the industry has a long history of manipulating nicotine levels in cigarettes to make them *more* addictive. Internal company documents from as far back as the 1950s expose the tobacco industry's extensive research on the importance of nicotine and how best to deliver nicotine to smokers and optimize its effects.<sup>83</sup> The documents demonstrate that they have known for decades that the key to their business is creating and sustaining dependence on nicotine, and they have purposely designed their products to do this effectively and efficiently. As U.S. District Judge Gladys Kessler concluded in her landmark 2006 civil racketeering judgment against the major cigarette manufacturers, *U.S. v. Philip Morris, Inc.*,

"... [C]igarette company defendants researched, developed, and implemented many different methods and processes to control the delivery and absorption of the optimum amount of nicotine which would create and sustain smokers' addiction. These methods and processes included, but were not limited to: altering the physical and chemical make-up of tobacco leaf blends and filler; maintaining or increasing the nicotine to tar ratio by changing filter design, ventilation and air dilution processes, and the porosity and composition of filter paper; altering smoke pH by adding ammonia to speed nicotine absorption by the central nervous system; and using other additives to increase the potency of nicotine."<sup>84</sup>

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<sup>79</sup> Tengs, T.O., et al., "The AMA proposal to mandate nicotine reduction in cigarettes: a simulation of the population health impacts," *Preventive Medicine*, 40: 170-180, 2005.

<sup>80</sup> Cigarettes with reduced nicotine are often referred to as reduced-nicotine cigarettes, very low nicotine content (VLNC) cigarettes, and de-nicotinized cigarettes.

<sup>81</sup> RJ Reynolds, "Our vision: We will achieve market leadership by transforming the tobacco industry," accessed August 8, 2017, <http://www.rjrt.com/transforming-tobacco/our-mission-and-vision/>.

<sup>82</sup> Philip Morris, "Our Manifesto: Designing a Smoke-Free Future," Accessed August 8, 2017, <https://www.pmi.com/who-we-are/designing-a-smoke-free-future>.

<sup>83</sup> Wayne, GF & Carpenter, CM, "Tobacco Industry Manipulation of Nicotine Dosing," *Handbook of Experimental Psychology* (192):457-85, 2009.

<sup>84</sup> *U.S. v. Philip Morris, USA, Inc.*, 449 F. Supp. 2d at 383-84 (D.D.C. 2006).

Finally, producing reduced-nicotine tobacco for other combusted tobacco products should be no more difficult than producing it for cigarettes.

**B. FDA Should Make the Effective Date of the Rule as Early as Possible.**  
**(ANPRM Section E, Question 5)**

The enormous public health benefits that would result from this rule should not be postponed any longer than absolutely necessary. Postponing the effective date of the rule only means that many hundreds of thousands of smokers and prospective smokers will unnecessarily have their lives shortened by an addiction that this rule could have prevented.

As indicated above, tobacco product manufacturers are already capable of extracting nicotine from tobacco and producing VLNC cigarettes. Growing low-nicotine tobacco is only one of several methods of complying with the standard. Thus, a tobacco product standard calling for a nicotine level to be set at non-addictive levels does not necessarily require “substantial changes to the methods of farming domestically grown tobacco;” thus, the statute does not require FDA to postpone the effective date of such a standard until two years after promulgation of the rule. Moreover, industry participants will have been on notice for a significant period of time that such a requirement would be imposed and prudent companies would have been making plans to comply with such a standard. Therefore, in no event should the implementation period be more than the one-year period contemplated for all product standards under Section 907 of the Tobacco Control Act.

Tobacco product manufacturers will no doubt make self-serving claims about how difficult, expensive, and time-consuming it would be to implement such a standard. FDA should view such claims skeptically given the clear economic interest the industry has in resisting or postponing measures designed to shrink the market for a highly profitable product. The public health benefits that will be gained from implementing the rule, however, make it imperative to make the rule effective as soon as possible. These benefits far outweigh the compliance costs the industry will experience.

It is also important for the rule to be applied simultaneously to all manufacturers. The continued availability of combusted products containing conventional levels of nicotine would undermine the effectiveness of the regulatory strategy and would create an opportunity for exempted manufacturers to earn windfall profits by continuing to supply high-nicotine level cigarettes. Manufacturers should not be enabled to undercut the effectiveness of important public health initiatives merely because they are small.

**C. Manufacturers, Distributors, and Retailers Should Not Be Allowed to Sell Off Existing Nonconforming Inventories. (ANPRM Section E, Question 6)**

Products currently on the market are both deadly and highly addictive. The public health imperatives that provide the foundations for replacing these products with VLNC cigarettes are inconsistent with permitting the continued sale of non-conforming inventories beyond the effective date of the rule. The presence of non-conforming product on the market after the effective date of the rule will only dilute the effectiveness of the rule and provide a wholly unjustified windfall to companies that have stockpiled an inventory in anticipation of its promulgation. Moreover, there is no unfairness to industry participants in prohibiting the sale of such inventories after the effective date of the rule. As noted above, all industry participants will have had a substantial period of prior notice of the promulgation of such a rule and will have had many opportunities to make arrangements to deal with the consequences.

In addition, permitting industry participants to sell off existing non-conforming inventories would create a massive incentive for companies to accumulate large inventories in the anticipation that they would be able to extract windfall profits from the sale of such products after the rule becomes effective.

Moreover, it is unlikely that any industry participants will be left with substantial inventories of nonconforming products. Current smokers are likely to buy up any available inventories of such products prior to the effective date of the rule. Thus, permitting industry participants at any level to sell off existing nonconforming inventories is not only contrary to the policies that underlie adoption of the rule, but is also wholly unnecessary to address any legitimate interest that a seller of tobacco products might have.

**D. FDA Should Require a Standard Method of Product Testing to Analyze Nicotine Levels. (ANPRM, Section D, Question 6)**

FDA asks whether, if it issues a product standard, it should require a standard method of product testing to analyze the nicotine levels in products subject to the standard. Adoption of a standard method of product testing would be helpful to ensure that all products are subject to the same standard and that the standard is actually being adhered to. FDA correctly observes that, “it is critical that the results from the test method used demonstrate a high level of specificity, accuracy, and precision in measuring a range of nicotine levels across a wide variety of tobacco blends and methods.”<sup>85</sup> In addition, FDA should require manufacturers to sample their products in a consistent manner to ensure that products do not contain excess levels of nicotine and to test each manufactured batch to ensure compliance.

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<sup>85</sup> 83 Fed. Reg. at 11820.

## V. Possible Countervailing Effects

### A. The Product Standard Should Prohibit the Sale or Distribution of Liquid Nicotine or Any Other Tobacco Product Designed to Supplement the Nicotine Content of Combusted Tobacco Products. (ANPRM Section F, Question 2)

FDA should assess the extent to which it would be feasible for smokers to supplement the nicotine content of combusted tobacco products through the use of liquid nicotine or another tobacco product. If such supplementation is feasible in a substantial number of cases, FDA should include in the rule a prohibition on the sale or distribution of liquid nicotine or any other tobacco product designed to supplement the nicotine content of combusted tobacco products.

### B. Illicit Trade (ANPRM Section F, Questions 3, 6, 7, 9)

These comments incorporate by reference the Comments filed by the undersigned organizations in Docket No. FDA-2018-N-0529, “Draft Concept Paper: Illicit Trade in Tobacco Products After Implementation of a Food and Drug Administration Product Standard,” 83 Fed. Reg. 11754 (March 16, 2018).

## VI. Other Considerations

### A. The Potential Consumer Surplus or Utility Loss from the Removal of Nicotine from Combusted Tobacco Products is Minimal in Light of the Availability of Other Sources of Nicotine and the Continued Availability of Tobacco Products. (ANPRM, Section G, Question 2)

The measurement of consumer surplus or utility loss in the context of the regulation of an addictive product, such as cigarettes, has been the subject of considerable debate. In 2014, a group of distinguished health economists presented to the U.S. Department of Health and Human Services and subsequently published a proposed formulation for the measurement of such consumer surplus or utility loss in this context.<sup>86</sup> After citing the fact that the large majority of smokers started smoking before the legal purchase age, regret the fact that they had started smoking and become addicted, and wished they could quit, the paper concluded:

“Indeed, the data strongly suggest that many smokers do not find smoking pleasurable, and that they derive little consumer surplus from smoking. Instead, most are struggling with or avoiding the withdrawal they would experience if they were able to stop smoking

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<sup>86</sup> Chaloupka FJ, et al., “An Evaluation of the FDA’s Analysis of the Costs and Benefits of the Graphid Warning Label Regulation,” *Tobacco Control*, 24:112-119, 2015.

and break an addiction they regret having ever started, facing psychological costs from being addicted and lacking the self-control to quit.”<sup>87</sup>

Accordingly, the paper recommended that, “nearly all of the lost pleasure from tobacco use, as represented by conventionally measured consumer surplus, should not be included as a cost in FDA analysis of the economic impact of its tobacco regulations.”<sup>88</sup> To the extent that measurement of consumer surplus or utility loss is required in the evaluation of regulations involving tobacco products, the undersigned organizations urge FDA to adopt the methods described in that paper.

In this case, there are further reasons why consumer surplus or utility loss, to the extent the concepts are relevant at all, would be minimal. If it is true that smokers smoke in order to obtain nicotine (an underlying premise of a nicotine products standard), to the extent that nicotine will remain available to them in other forms, either through appropriately regulated e-cigarettes, NRT products, or otherwise, means that the “pleasure” of receiving nicotine is not being denied to them. To the extent that these product satisfy the need for nicotine, there is no “lost pleasure.” Moreover, to the extent that smokers can satisfy the need for nicotine at a far lower cost to their health indicates that individual smokers will realize a large net economic gain.

Moreover, cigarettes and other combusted tobacco products will remain available for sale. To the extent that smokers derive pleasure from smoking apart from satisfying their need for nicotine, they will continue to be able to purchase cigarettes and other combusted products. Having access to both nicotine and combusted tobacco products, it is questionable whether smokers will experience any loss of consumer surplus, even assuming that such surplus is generated by smoking.

**B. FDA Should Consider Externalities, Such as the Reduction in Secondhand Smoke, in Evaluating the Consequences of the Rule (ANPRM Section G, Question 6)**

If, as expected, a product standard reducing the level of nicotine in cigarettes and other combusted products substantially reduces the number of cigarettes and other combusted tobacco products smoked, there will be a corresponding reduction in environmental tobacco smoke and in the death and disease resulting from non-smokers’ exposure to such smoke. FDA estimates that from 2005 to 2009, an estimated 7,330 lung cancer and 33,950 heart disease deaths were attributable to secondhand smoke and that secondhand tobacco smoke causes premature death and disease in children and adults who do not smoke.<sup>89</sup> It is apparent that a reduction in environmental tobacco smoke would reduce the burden of death and disease for non-smokers and provide a substantial public health benefit. Any analysis of the effects of such a rule should

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<sup>87</sup> *Id.*

<sup>88</sup> *Id.*

<sup>89</sup> 83 Fed. Reg. at 11825.

consider the benefits to non-smokers that would result through a reduction in death and disease attributable to environmental tobacco smoke.

### **C. Post-market Surveillance is Critical**

Critical to the success of a nicotine reduction policy is a rigorous and comprehensive post-market surveillance and product-testing program to monitor for any unintended tobacco use patterns and to identify any changes in product design that may limit the effectiveness of reduced nicotine content.

Respectfully submitted,

Action on Smoking and Health  
American Academy of Family Physicians  
American Academy of Oral and  
Maxillofacial Pathology  
American Association for Dental Research  
American Association for Respiratory Care  
American Cancer Society Cancer Action  
Network  
American College of Cardiology  
American College of Physicians  
American College of Preventive Medicine  
American Heart Association  
American Lung Association  
American Medical Association  
American Medical Student Association  
American Psychological Association  
American Public Health Association  
American School Health Association  
American Society of Addiction Medicine  
American Society of Clinical Oncology  
Americans for Nonsmokers' Rights  
Association of State and Territorial Health  
Officials  
Big Cities Health Coalition  
Campaign for Tobacco-Free Kids  
Community Anti-Drug Coalitions of  
America  
Counter Tools

Eta Sigma Gamma - National Health  
Education Honorary  
Mesothelioma Applied Research Foundation  
National Association of County and City  
Health Officials  
National Hispanic Medical Association  
National Network of Public Health Institutes  
Oncology Nursing Society  
Oral Health America  
Prevention Institute  
Public Health Law Center | Tobacco Control  
Legal Consortium  
Public Health Solutions  
Society for Cardiovascular Angiography and  
Interventions  
Society for Public Health Education  
Students Against Destructive Decisions  
The Society for State Leaders of Health and  
Physical Education  
Trust for America's Health  
Truth Initiative