

**Listing of Ingredients in Tobacco Products –
Revised Draft Guidance for Industry
Docket Number FDA-2009-D-0524**

Lauren K. Lempert, Lucy Popova*, Bonnie Halpern-Felsher, Benjamin Chaffee, Neal Benowitz, Gideon St. Helen, Eunice Neeley, Stanton A. Glantz
University of California, San Francisco TCORS
*Georgia State University, School of Public Health

November 28, 2016

FDA's revised draft guidance on "Listing of Ingredients in Tobacco Products"¹ discusses the application of the Family Smoking Prevention and Tobacco Control Act's section 904 ingredient submission requirements to newly deemed tobacco products. Tobacco product ingredient submissions are an essential component of FDA's mandate under the Tobacco Control Act to protect the public health, reduce tobacco use and its harms, and inform consumers of the hazardous substances in tobacco products. Since the first edition of this guidance was issued in November 2009,² the public health community has become aware of new information that is relevant to tobacco product ingredients that should inform ingredients listing requirements and be incorporated into the revised guidance as described below.

1. FDA should require submission of information about tobacco product packaging along with other required information about additives, tobacco blends, flavorings, and other components and parts.

All additives, components, and parts are "ingredients" that must be submitted under section 904(a), and therefore are required to be submitted in ingredients lists. FDA defined "additive" in the draft guidance (page 4) to include "any substance the intended use of which results or may reasonably be expected to result in ... affecting the characteristic of any tobacco product (including any substances intended for use as... coloring or ... packaging...)" FDA defined (page 4) "component or part" for the purposes of this guidance as "any software or assembly of materials intended or reasonably expected: (1) to alter or affect the tobacco product's performance...or characteristics..." Further, FDA acknowledged (page 8) that an ingredient may function as an agent that "affects perception" of the smoking experience. We now know that companies manipulate consumers' perceptions of the taste, strength, and health effects of cigarettes by changing the color of cigarette packaging, so that even without making changes to the tobacco blends or flavorings, consumers perceive the taste and effect of cigarettes in certain packages differently (stronger, fuller flavored, lighter, less harmful) from cigarettes in other packs,^{3, 4} and consumers ascribe differences in risk based on packaging.⁵

Package characteristics including design, colors and product descriptors provide information to consumers about product characteristics and health risks⁶⁻¹⁰ Brand "descriptors" such as certain words (e.g., smooth), colors (e.g., silver, gold), or

numbers (lower numbers) are used to denote flavor and taste. Brand descriptors on packages can infer “lower tar numbers” and promote sensory perceptions of ‘lighter’ smoke and impart relative health risk messages to both smokers and nonsmokers. Bansal-Travers et al. found⁵ that smokers of low-tar brands were more likely than smokers of full flavor cigarettes to rate the packs with lighter colors and misleading brand descriptors as lower in tar delivery and posing less risk to health, indicating that at least for some smokers, these package features influence purchasing choices. Adolescents ascribe different characteristics associated with Marlboro cigarette pack colors (e.g., smooth, low-tar) in line with industry definitions (McKelvey and Halpern-Felsher, in preparation).

In light of this new evidence, FDA should require submission of information about packaging for new submissions *and for any changes in packaging* since previous submissions.

Section 904(c) requires submission of information whenever any additive is changed. Based on new scientific evidence about how packaging changes consumers’ perceptions of the products inside the packs, just as changes in tobacco blends and flavorings do, any changes in packaging for all tobacco products, including for newly deemed tobacco products, should require submission of ingredient information, including information about the packaging. FDA incorrectly interprets section 904(a)(1) by suggesting that cigarettes sold in different packaging may be otherwise “identical” and therefore do not required a separate submission of ingredients. The scientific evidence³ on the impact of package changes does not support this interpretation. ***Because any change in packaging has the potential to change consumers’ perceptions about the tobacco products inside the pack, FDA should require submission of information about these pack changes along with other ingredients submissions.***

2. FDA should require submission of detailed information about all ingredients, components, and parts associated with hookah and similar tobacco products, including the types and amounts of charcoal and the types and amounts of charcoal emissions, and the nature of the hookah tobacco including the types and amounts of fruit, molasses, and other hookah tobacco additives and flavorings and the types and amounts of hookah tobacco emissions.

The combustion products of charcoal and hookah tobacco create toxic emissions that are hazardous to the health of hookah users and bystanders.¹¹⁻¹³ Charcoal is produced by incomplete combustion of wood. As in incomplete combustion of other organic materials, polycyclic aromatic hydrocarbons (PAHs) are produced. It is well known that burning charcoal produces large amounts of CO. Burning charcoal also produces benzene,¹⁴ a carcinogen associated with increased incidence of leukemia. One study of hookah emissions showed that charcoal emissions were the primary source of CO and carcinogenic PAHs; 90% of CO and 75-92% of 4- and 5-ring PAHs

(the heavy molecular PAHs) originated from the charcoal.¹⁵ Hookah smoke contains high levels of toxic compounds, including tar, carbon monoxide,¹⁶⁻¹⁸ heavy metals, and carcinogens. It is possible that different kinds of charcoal used in diverse hookah products generate toxic emissions of varying types and amounts. Several studies have measured tobacco-related toxicants in hookah smoke, including polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs) such as formaldehyde, acetone, and acrolein, and carcinogenic tobacco-specific nitrosamines (TSNAs).¹⁹⁻²¹ Hookah smoking machine studies indicated that the amount of water pipe tobacco used in a single hookah smoking session produced 100-fold more tar, 4-fold more nicotine, 11-fold more CO, and 2- to 5-fold more polycyclic aromatic hydrocarbons than did a single cigarette.²⁰

While the unburned fruit and molasses ingredients in hookah tobacco may be benign when eaten, when these ingredients are combusted the emissions are dangerous. Moreover, hookah smokers may actually inhale more tobacco smoke than cigarette smokers do because of the large volume of smoke they inhale in one smoking session.^{22, 23} Many users, especially youth, believe that hookah use is less harmful than cigarette smoking.²⁴ ***FDA should require submission of specific information about the hookah ingredients, including in particular the health impacts of the combustion products and emissions generated by the hookah charcoal and by the hookah tobacco ingredients, flavorings, and additives. Additionally, the industry should be required to provide detailed information about the hookah heating coil materials and construction, the battery and resulting wattage, and any and all other information related to the heating and combustion of hookah tobacco, as these materials can affect the nature and toxicity of the aerosol emitted. This information is essential to protect the public health and to inform consumers and the scientific community.***

3. FDA should require submission of detailed information about the effects of flavors in increasing initiation and reducing cessation of tobacco products

Significant scientific evidence shows that flavors in tobacco products, including newly deemed products such as cigars and electronic cigarettes, increases initiation of tobacco use, especially among youth, and decreases cessation. A 2013 study found that 18.5% of tobacco users report using flavored products, dual use of menthol and flavored product use was as high as 72% for chewing tobacco, and younger adults were more likely to use flavored tobacco products.²⁵ A 2016 systematic review of 32 individual studies concluded that nonmenthol flavored tobacco is more likely to be used by youth and young adults, is viewed more favorably than unflavored tobacco among adult and adolescent tobacco users, and is more appealing than unflavored tobacco to non-tobacco users.²⁶ Another 2016 systematic review of 40 studies examining the impact of non-menthol flavors in tobacco products on tobacco use perceptions and behaviors among youth, young adults, and adults found that flavors

in most tobacco products appear to play a key role in how users and non-users, especially youth, perceive, initiate, progress, and continue using tobacco products.²⁷ Additionally, an FDA review concluded that menthol cigarettes likely pose a greater risk to the public than non-menthol cigarettes,²⁸ noting greater use by younger, less experienced smokers, racial-ethnic minorities, and in low socio-economic status groups,^{29, 30} as well as evidence suggesting that menthol in cigarettes promotes smoking initiation, progression to established smoking, greater nicotine dependence, and reduced smoking cessation success.^{31, 32} Laboratory analysis of multiple non-cigarette tobacco products identified the same sweeteners³³ and chemical flavorings³⁴ found in popular candies, and levels in some tobacco products could exceed acceptable daily intakes.³⁵ It is highly plausible that menthol, as well as nonmenthol flavors, found in non-cigarette tobacco products increase the risk similarly to menthol in cigarettes.

There is evidence that flavors are a major driver of tobacco sales in the youth market, and that youth want strong and intense flavors in the products they consume. The 2012 Surgeon General report, *Preventing Tobacco Use Among Youth and Young Adults*,³⁶ observed that the use of tobacco products such as cigars and smokeless tobacco that are available in flavors have increased among high school students. The cigars preferred most by adolescents and young adults are flavored (peach, grape, apple, and chocolate). Tobacco manufacturers have used menthol and cherry flavored smokeless products as part of a “graduation strategy” with low free nicotine content to encourage new users to start with particular products and progress to others with higher levels of free nicotine.³⁶ With many of these flavored products available on the market, smokeless tobacco use has been increasing among adolescents.³⁷ Oliver and colleagues found that mint flavored smokeless tobacco products play a role in the initiation and maintenance of smokeless tobacco use.³⁸ A majority of first and current choice of smokeless tobacco products was flavored, and a significant number of those who initiated use with unflavored products eventually switched to flavored products, specifically mint or wintergreen, to sustain use.³⁸ With increased manufacture of flavored moist snuff by 72% between 2005 and 2011, flavored moist snuff products contributed to 59.4% of the growth.³⁹ Research on flavors has focused mostly on cigarettes⁴⁰⁻⁴³ and on cigars,⁴⁴⁻⁴⁷ and almost all examine prevalence and use patterns.^{48, 49}

Known inhalation toxicants such as cinnamaldehyde, diacetyl, and other aldehydes contained in flavor chemicals raise particular public health concern.

FDA should require submission of detailed information about the chemical constituents of flavorings and flavor enhancers, including all industry research that investigates the behavioral and health impacts of flavors.

- 4. FDA should use its authority under section 904(b) to demand information and any or all documents from manufacturers on their research activities and findings concerning: (a) the health, toxicological, behavioral, psychological, and addictive effects of tobacco products and**

their ingredients, additives, components, and parts; (b) whether tobacco product ingredients are related to that product's reduction or increase in risk to health; and (c) how these products are marketed and market research on how marketing practices affect consumers' perceptions of the products' harms or health impacts.

FDA should require submission of industry studies demonstrating how tobacco product ingredients and additives such as ammonia and sugars affect smoke pH and potentially increase the addictive power of nicotine in tobacco products.⁵¹ FDA should require industry studies on how menthol⁵² and flavors promote initiation and reduce cessation, especially among youth. Adolescents are more likely to initiate with flavored tobacco products, and in particular prefer fruit and dessert flavors (e.g., chocolate, cherry), as well as mint flavors.^{36-39, 50} FDA should require that manufacturers submit their market research studies on how particular marketing strategies attract youth and other targeted populations such as point-of-sale ads and packaging using colors that mimic candy ads and packaging, internet ads, and social media platforms.

Adolescents and young adults in particular have a difficult time understanding what addiction means, including lacking the understanding that addiction means that it will be difficult to quit and not recognizing how quickly and how little they need to smoke to become addicted.^{53, 54} Research shows that adolescents display optimism regarding their ability to quit smoking as well as skepticism over the seriousness of nicotine addiction. A longitudinal study in which adolescents were followed for three years found that they were optimistically biased, believing that their own risk of addiction is lower than risk of addiction of "comparable others."⁵⁵ Qualitative studies also show that while youth and young adults are aware of the risk of nicotine addiction, they display a great deal of uncertainty over what nicotine addiction actually entails. In particular, adolescents do not realize that "addiction" means it is very difficult to quit using these products, and that many of the "pleasures" of tobacco use, such as relaxation, are simply the results of self-medication (with nicotine) to treat the symptoms of acute nicotine withdrawal.^{53, 54} Adolescents often believe that all electronic cigarettes do not contain nicotine, and that they are not addictive.⁵⁰

Nitrosamines are carcinogenic, combustion products of burning sugars significantly affect smoke PH,⁵¹ and many flavorings contain aldehydes that may be toxic.^{56, 57} Therefore, FDA should require the industry to submit detailed lists of nitrosamines, sugars, and aldehyde levels, as well as industry studies about the potential toxicity and/or carcinogenicity of nitrosamines, sugar combustion products, and aldehyde levels. Additionally, FDA should require submission of lists and industry studies of any other harmful or potentially harmful constituents in all tobacco products, including newly deemed products.

5. FDA must make submitted listings of ingredients easily accessible to and in a format that is understandable by the lay public and scientific community

To meet its obligation under the Family Smoking Prevention and Tobacco Control Act (FSPTCA) to inform the public about the hazards and health impacts of tobacco use and in particular the harmful and potentially harmful constituents, FDA should publish all the ingredients information that is submitted pursuant to FSPTCA section 904(a), as well as any additional data or research that companies provide in response to separate FDA requests pursuant to FSPTCA section 904(b). The revised draft guidance fails to address this critical mandate. ***FDA should require, not merely “strongly encourage” (page 13), that all ingredient information is submitted electronically so it can easily and immediately be made available to the public.***

Currently, it is virtually impossible for even public health researchers, let alone the lay public, to access this critically important information, and they must often rely on FOIA requests that are time-consuming and expensive for all parties. It is essential that manufacturers submit this information in a manner that is consistent and “useful to the public and not misleading to laypersons.” (page 12). ***FDA should revise its draft guidance to explicitly describe how it will make the submitted information available to the public.***

6. While FDA must maintain the confidentiality of “nonpublic trade secret or confidential commercial information,” neither the FD&C Act, the Trade Secrets Act, nor the Freedom of Information Act requires FDA to conceal from the public information that is neither a trade secret nor confidential commercial information

A peer-reviewed study⁵⁸ based on previously secret tobacco industry documents shows that major tobacco companies routinely reverse-engineer their competitors’ tobacco products. This study analyzed 100 examples of seven major tobacco companies’ reverse engineering reports of their competitors’ brands and found that these reverse engineering reports contain detailed data for as many as 142 different measurements, including physical parameters of the cigarettes, tobacco types, humectants, additives, flavorings, and smoke constituents of competitors’ cigarettes.⁵⁸ (These reverse engineering reports are publicly available at <https://www.industrydocumentslibrary.ucsf.edu/tobacco/>.) This information, including ingredient changes over time and company decisions regarding ingredients, has been distributed to employees and top managers both domestically and internationally. Therefore, this information is neither secret nor commercially valuable, and thus does not meet the legal definition of a “trade secret” entitled to trade secret protection. Rather, this information is only being kept secret from the scientific community and from lay people who use the tobacco products. FDA should not uncritically accept trade secret claims connected with ingredients information submitted by tobacco companies and determine whether the

information should indeed be considered “trade secrets” entitled to protection. The burden is on the tobacco companies to demonstrate that specific pieces of information are entitled to trade secret protection.

In the case of tobacco products that contain proprietary blends and formulas that may be considered and proven to be trade secrets, FDA can and should still make publicly available the identity of the product ingredients without revealing the blends or formulas, thereby protecting the trade secrets as required by law. For example, the formula for Coca-Cola is recognized to be confidential and a strictly protected trade secret; nevertheless, cans of Coke contain an ingredients and nutrition facts label that includes a list of the product ingredients (carbonated water, high fructose corn syrup, caramel color, phosphoric acid, natural flavors, caffeine) as well as the amounts of total fat, sodium, total carbohydrates, sugars, protein, and calories, and this information is easily found online. Similarly, FDA should make all tobacco product information submitted by the companies available to the public online, and should consider requiring descriptive information about ingredients on packages or on package inserts or onserts.

7. FDA's compliance policy for ingredient list submissions is reasonable

FDA's compliance policy for when lists of ingredients for newly deemed tobacco products must be submitted (February 8, 2017 for products that were first introduced into interstate commerce before August 8, 2016, August 8, 2017 for small-scale manufacturers; for products first marketed after August 8, 2016, at least 90 days before the product is introduced into interstate commerce) is reasonable because it gives manufacturers sufficient time to collect and submit the required information. To protect the public health, FDA should enforce section 904 if these requirements are not met by the specified dates.

References

1. U.S. Food and Drug Administration, Center for Tobacco Products. Listing of Ingredients in Tobacco Products (Revised): Guidance for Industry; Draft Guidance. 2016, *available at* <https://www.regulations.gov/document?D=FDA-2009-D-0524-0027>.
2. U.S. Food and Drug Administration, Center for Tobacco Products. Guidance for Industry: Listing of Ingredients in Tobacco Products. 2009, *available at* <https://www.regulations.gov/document?D=FDA-2009-D-0524-0025>.
3. Lempert LK and Glantz S. Packaging colour research by tobacco companies: the pack as a product characteristic. *Tob Control*. 2016.
4. Connolly GN and Alpert HR. Has the tobacco industry evaded the FDA's ban on 'Light' cigarette descriptors? *Tob Control*. 2014;23:140-5.
5. Bansal-Travers M, Hammond D, Smith P and Cummings KM. The Impact of Cigarette Pack Design, Descriptors, and Warning Labels on Risk Perception in the US. *Am J Prev Med*. 2011;40:674-682.

6. Hammond D, Dockrell M, Arnott D, Lee A and McNeill A. Cigarette pack design and perceptions of risk among UK adults and youth. *European Journal of Public Health*. 2009;19:631-637.
7. Hammond D and Parkinson C. The impact of cigarette package design on perceptions of risk. *J Public Health (Oxf)*. 2009;31:345-53.
8. Wakefield M, Morley C, Horan JK and Cummings KM. The cigarette pack as image: new evidence from tobacco industry documents. *Tob Control*. 2002;11:I73-I80.
9. Borland R, Fong GT, Yong H-H and et al. What happened to smokers' beliefs about light cigarettes when "light/mild" brand descriptors were banned in the UK? Findings from the International Tobacco Control (ITC) Four Country Survey *Tob Control*. 2008;17(4):256-62.
10. Wakefield M and Letcher T. My pack is cuter than your pack. *Tob Control* 2002;11(2):154.
11. St.Helen G, Benowitz NL, Dains KM and et al. Nicotine and carcinogen exposure after water pipe smoking in hookah bars. *Cancer Epidemiol Biomarkers Prev*. 2014;23(6):1055-66.
12. Kassem NO, Daffa RM, Liles S, Jackson SR, Kassem NO, Younis MA, Mehta S, Chen M, Jacob P, 3rd, Carmella SG, Chatfield DA, Benowitz NL, Matt GE, Hecht SS and Hovell MF. Children's exposure to secondhand and thirdhand smoke carcinogens and toxicants in homes of hookah smokers. *Nicotine Tob Res*. 2014;16:961-75.
13. Kassem NO, Kassem NO, Jackson SR, Liles S, Daffa RM, Zarth AT, Younis MA, Carmella SG, Hofstetter CR, Chatfield DA, Matt GE, Hecht SS and Hovell MF. Benzene uptake in Hookah smokers and non-smokers attending Hookah social events: regulatory implications. *Cancer Epidemiol Biomarkers Prev*. 2014;23:2793-809.
14. Olsson M and Petersson G. Benzene emitted from glowing charcoal. *Science of the Total Environment*. 2003;303:215-220.
15. Monzer B, Sepetdjian E, Saliba N and Shihadeh A. Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food Chem Toxicol*. 2008;46(9):2991-5.
16. Ashurst JV, Urquhart M and Cook MD. Carbon monoxide poisoning secondary to hookah smoking *J Ameri Osteopathic Association* 2012;112:686-688.
17. Cavus UY, Rehber ZH and Ozeke O. Carbon monoxide poisoning associated with Narghile use. *Emergency Medicine Journal*. 2010;27 406.
18. Lim BL, Lim GH and Seow E. Case of carbon monoxide poisoning after smoking shisha. *Int J Emergency Med*. 2010;11:121-122.
19. Schubert J, Heinke V, Bewersdorff J, Luch A and Schulz TG. Waterpipe smoking: the role of humectants in the release of toxic carbonyls. *Arch Toxicol*. 2012;86:1309-16.
20. Shihadeh A and Saleh R. Polycyclic aromatic hydrocarbons, carbon monoxide, "tar", and nicotine in the mainstream smoke aerosol of the narghile water pipe. *Food Chem Toxicol*. 2005;43:655-61.
21. Schubert J, Hahn J, Dettbarn G and et al. Mainstream smoke of the waterpipe: does this environmental matrix reveal as significant source of toxic compounds? *Toxicol Lett* 2011;205(3):279-84.

22. Haddad L, El-Shahawy O, Ghadban R and et al. Waterpipe Smoking and Regulation in the United States: A Comprehensive Review of the Literature *Int J Environ Res Public Health*. 2015;12(6):6115-6135.
23. Everts S. What's Hookah, And Is It Healthier Than Smoking A Cigarette? *Chemical & Engineering News*, Vol. 93, Issue 25, p. 41.
24. Roditis M, Delucchi K, Cash D and Halpern-Felsher B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ Across Tobacco Products. *J Adolesc Health*. 2016;58:558-66.
25. Villanti AC, Richardson A, Vallone DM and Rath JM. Flavored tobacco product use among US young adults. *Am J Prev Med*. 2013;44(4):388-391.
26. Feirman SP, Lock D, Cohen JE and et al. Flavored Tobacco Products in the United States: A Systematic Review Assessing Use and Attitudes. *Nicotine Tob Res*. 2016;18(5):739-49.
27. Huang L-L, Baker HM, Meernik C and et al. Impact of non-menthol flavours in tobacco products on perceptions and use among youth, young adults and adults: a systematic review. *Tob Control Published Online First: [21 Nov 2016]* doi:101136/tobaccocontrol-2016-053196. 2016.
28. Food and Drug Administration. Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes. July 2013
29. Hersey JC, Ng SW, Nonnemaker JM and et al. Are menthol cigarettes a starter product for youth? *Nicotine Tob Res*. 2006;8(3):403-13.
30. Giovino GA, Villanti AC, Mowery PD and et al. Differential trends in cigarette smoking in the USA: is menthol slowing progress? *Tob Control*. 2015;24(1):28-37.
31. Garten S and Falkner RV. Role of mentholated cigarettes in increased nicotine dependence and greater risk of tobacco-attributable disease. *Prev Med*. 2004;38(6):793-8.
32. Nonnemaker J, Hersey J, Homsy G and et al. Initiation with menthol cigarettes and youth smoking uptake. *Addiction*. 2013;108(1):171-8.
33. Miao S, Beach ES, Sommer TJ and et al. High-intensity sweeteners in alternative tobacco products. *Nicotine Tob Res*. 2016;18(11):2169-2173.
34. Brown JE, Luo W, Isabelle LM and Pankow JF. Candy flavorings in tobacco. *N Engl J Med*. 2014;370(23):2250-2.
35. Chen C, Isabelle LM, Pickworth WB and Pankow JF. Levels of mint and wintergreen flavorants: smokeless tobacco products vs. confectionery products. *Food Chem Toxicol*. 2010;48(2):755-63.
36. U.S. Department of Health and Human Services. Preventing Tobacco Use Among Youth and Young Adults. A Report of the Surgeon General. 2012
37. Johnston L, O'Malley P, Bachman J and Schulenberg J. Monitoring the Future national survey results on drug use, 1975-2010. Volume I: Secondary school students. 2011.
38. Oliver AJ, Jensen JA, Vogel RI and et al. Flavored and nonflavored smokeless tobacco products: rate, pattern of use, and effects. *Nicotine Tob Res*. 2013:88-92.
39. Delnevo CD, Wackowski OA, Giovenco DP and et al. Examining market trends in the United States smokeless tobacco use: 2005–2011. *Tob Control* 2014;23(2):107-12.

40. Carpenter CM, Wayne GF, Pauly JL and et al. New cigarette brands with flavors that appeal to youth: tobacco marketing strategies. *Health Affairs* 2005;24(6):1601-10.
41. Ashare RL, Hawk Jr. LW, Cummings KM and et al. Smoking expectancies for flavored and non-flavored cigarettes among college students. *Addictive Behaviors*. 2007;32(6):1252-61.
42. Klein SM, Giovino GA, Barker DC and et al. Use of flavored cigarettes among older adolescent and adult smokers: United States, 2004–2005. *Nicotine Tob Res*. 2008;10(7):1209-14.
43. Lewis MJ and Wackowski O. Dealing with an innovative industry: a look at flavored cigarettes promoted by mainstream brands. *Amer J Pub Health* 2006;96(2):244.
44. Delnevo CD and Hrywna M. Clove cigar sales following the US flavoured cigarette ban. *Tob Control*. 2015;24:e246-50.
45. King BA, Tynan MA, Dube SR and et al. Flavored little cigar and flavored cigarette use among US middle and high school students *J Adolescent Health* 2014;54(1):40-46.
46. King BA, Dube SR and Tynan MA. Flavored cigar smoking among US adults: findings from the 2009–2010 National Adult Tobacco Survey. *Nicotine Tob Res*. 2013;15(2):608-14.
47. Voelker R. Teen Smokers Turn to Flavored Cigars. *JAMA*. 2014;311(3):236.
48. Minaker LM, Ahmed R, Hammond D and Manske S. Flavored Tobacco Use Among Canadian Students in Grades 9 Through 12: Prevalence and Patterns From the 2010–2011 Youth Smoking Survey. *Prev Chronic Dis* 2014;11:140094.
49. Regan AK, Dube SR and Arrazola R. Smokeless and flavored tobacco products in the U.S.: 2009 Styles survey results. *Am J Prev Med*. 2012;42(1):29-36.
50. Ramos M, Roditis M, Ramamurthi D and Halpern-Felsher B. Qualitative Analysis of Adolescents' Appeal of Various Tobacco Products, presented at the second NIH Tobacco Regulatory Science Conference, May 16-18 2016 and at the Pediatrics Academic Societies Meeting, April 30-May 2 2016.
51. Talhout R, Opperhuizen A and van Amsterdam J. Sugars as tobacco ingredient: Effects on mainstream smoke composition. *Food and Chemical Toxicology*. 2006;44(11):1789–1798.
52. Yerger VB. Menthol's potential effects on nicotine dependence: a tobacco industry perspective. *Tob Control*. 2011;20 Suppl 2:ii29-36.
53. Roditis M, Lee J and Halpern-Felsher B. Adolescent (Mis)Perceptions about Nicotine Addiction: Results from a Mixed-Methods Study. *Health Education & Behavior*. 2016;43(2) 156-64.
54. Lee J and Halpern-Felsher B. What does it take to be a smoker? Adolescents' characterization of different smoker types. *Nicotine Tob Res*. 2011;13:1106-1113.
55. Popova L and Halpern-Felsher B. A Longitudinal Study of Adolescents' Optimistic Bias about Risks and Benefits of Cigarette Smoking. *Amer J Health Behavior*. 2016;40(3):341-351.
56. Yeager RP, Kushman M, Chemerynski S, Weil R, Fu X, White M, Callahan-Lyon P and Rosenfeldt H. Proposed Mode of Action for Acrolein Respiratory Toxicity Associated with Inhaled Tobacco Smoke. *Toxicol Sci*. 2016;151:347-64.

57. DeJarnett N, Conklin D, Riggs D and et al. Acrolein Exposure Is Associated With Increased Cardiovascular Disease Risk. *JAHA*. 2014;3.
58. Velicer C, Lempert LK and Glantz S. Cigarette company trade secrets are not secret: an analysis of reverse engineering reports in internal tobacco industry documents released as a result of litigation. *Tob Control*. 2015;24:469-80.