

A SCIENCE AND EVIDENCE BASED NICOTINE TOBACCO PRODUCT STANDARD

Donna Smith

Senior Principal Scientist

Regulatory Sciences

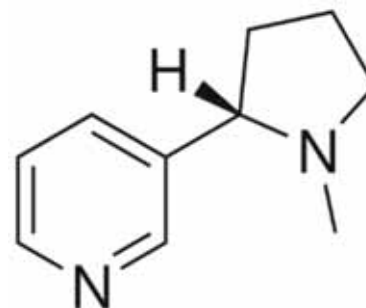


Altria
Altria Client Services

FDA's 2017 Policy Shift



- Endorsement of harm reduction and the continuum of risk
- Policy: encourage cigarette smokers to switch to less risky products
- Drastically reduce nicotine to minimal levels to force the migration of cigarette smokers and reduce initiation



Altria Client Services | Donna Smith | September 17, 2018 | Final | TSRC 2018 | 2

FDA Published ANPRM on Nicotine Content

“FDA is particularly interested in comments about the merits of nicotine levels like 0.3, 0.4 and 0.5 mg nicotine/g of tobacco filler, as well as other levels of nicotine.”

Source: Fed. Reg. Vol 83, No. 52/11820



11818 Federal Register / Vol. 83, No. 52 / Friday, March 16, 2018 / Proposed Rules

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
21 CFR Part 1130
(Docket No. FDA-2017-A-418)
IR 9916; A18E

Tobacco Product Standard for Nicotine Level of Combusted Cigarettes
AGENCY: Food and Drug Administration, HHS.

ACTION: Advance notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing this advance notice of proposed rulemaking (ANPRM) to obtain information for consideration in developing a tobacco product standard to set the maximum nicotine level for cigarettes. Because tobacco-related harms ultimately result from addiction to the nicotine in such products, ensuring regular use and exposure to low-nicotine, FDA is considering taking this action to reduce the level of nicotine in these products so they are minimally addictive or nonaddictive, using the best available science to determine a level that is appropriate for the protection of the public health. FDA is using the term “nonaddictive” in this document specifically in the context of a potentially nonaddictive cigarette. We acknowledge the highly addictive potential of nicotine itself depending upon the route of delivery. As discussed elsewhere in this document, questions remain with respect to the precise level of nicotine in cigarettes that might render them either minimally addictive or nonaddictive for specific members or segments of the population. We envision the potential circumstances where nicotine levels in cigarettes do not spur or sustain addiction for some portion of potential smokers. This could give adults who use the choice and ability to quit more easily, and it could help to prevent experimentation (mainly youth) from initiating regular use and becoming regular smokers. The scope of products covered by any potential product standard will be less than for comment in the ANPRM. Any additional scientific data and research relevant to the empirical basis for regulatory decisions related to a nicotine tobacco product standard is another issue for comment in the ANPRM.

DATES: Submit either electronic or written comments on the ANPRM by June 14, 2018.

ADVERTISE: You may submit comments as follows: Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before June 14, 2018. The <http://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of June 14, 2018. Comments received by mail/hand delivery/runner (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions
 Submit electronic comments in the following way:
 • Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's social security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
 • If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed in “Written/Paper Submissions” and “Instructions.”

Written/Paper Submissions
 Submit written/paper submissions as follows:
 • Mail/Hand delivery/Counter (for written/paper submissions): Dockets Management Staff (HFA-410), Food and Drug Administration, 5630 Fishers Lane, RM. 1061, Rockville, MD 20852.
 • For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2017-A-418 for “Tobacco Product Standard for Nicotine Level of Certain Tobacco Products.” Received comments, those filed in a timely manner (see **ADVERTISE**), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <http://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.
 • Confidential Submissions.—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 101.20 and other applicable disclosure law. For more information about FDA's posting of comments to public docket, see 21 CFR 101.20, September 16, 2012, or access the information at: <http://www.gpo.gov/fdsys/pkg/FR-2012-09-16/pdf/2012-09-16.pdf>.
 Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, listed in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, RM. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:
 Carla Voss, Center for Tobacco Products, Food and Drug Administration, 10805 New Hampshire Ave., Silver Spring, MD 20903, 1-877-CYF-3373, carla.voss@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

Table of Contents
 I. Executive Summary
 A. Purpose of the Advance
 B. Summary of the Major Issues Related to the ANPRM
 C. Background



ANPRM Nicotine Content Focus

- “A 2013 survey paper noted that researchers initially estimated that reducing the total nicotine content of cigarettes to 0.5 milligrams (mg) per rod would minimize addictiveness and that a ‘more recent analysis suggests that the maximum allowable nicotine content per cigarette that minimizes ... addiction may be lower.’”

Source: Fed. Reg. Vol 83, No. 52/11819

- “We specifically request comment regarding this paper’s conclusions...”

Source: Fed. Reg. Vol 83, No. 52/11819



The More Recent Analysis

HHS Public Access
Author manuscript
Tab Control. Author manuscript; available in PMC 2015 October 24.

Published in final edited form in:
Tab Control. 2015 October; 19(5): e1-02. doi:10.1134/n.2009.00104.

Nicotine Reduction Revisited: Science and Future Directions

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Abstract

Reduction of nicotine levels in cigarettes and other tobacco products is now possible with the passage of the Family Smoking Prevention and Tobacco Control Act (FSPTCA) in 2009 giving the U.S. Food and Drug Administration authority to regulate tobacco products, and with Article 9-11 of the World Health Organization Framework Convention on Tobacco Control [1-2]. Both regulatory approaches allow establishing product standards for tobacco constituents, including nicotine. The FSPTCA does not allow nicotine levels to be decreased to zero, although FDA has the authority to reduce nicotine yields to very low, presumably non-addicting levels. The proposal to reduce levels of nicotine to a level that is non-addicting was originally proposed in 1994 [3]. Reduction of nicotine in tobacco products could potentially have a profound impact on reducing tobacco-related morbidity and mortality. To examine this issue, two meetings were convened in the United States with non-tobacco-industry scientists of varied disciplines, tobacco control policy-makers and representatives of governmental agencies. This article provides an overview of the current science in the area of reduced nicotine content cigarettes and key conclusions and

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Dorothy Hatsukami has received grant funding from State Replacememts to conduct nicotine-reduce clinical trials. Jack Henningfield provides consulting support to GlaxoSmithKline Consumer Health through Finney Associates as an exclusive basis on issues related to tobacco dependence treatment. Ken LeSage served as a consultant for and nicotine replacement product, and served as an expert witness in litigation against tobacco companies. Neal Benowitz serves as a consultant for Pfizer and as an expert witness in litigation against tobacco companies. Mitch Zeller provides consulting support to GlaxoSmithKline Consumer Health through Finney Associates as an exclusive basis on issues related to tobacco dependence treatment. Kenneth Perkins has served as a consultant to Cigara Sciences.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive license (or non-exclusive license for government employees) to a publisher to publish the article in print and/or in electronic form in any journal or database, and any other FSPTCA products to explore all subsidiary rights, as set out in the license.

- The paper makes no attempt to identify a nicotine threshold of addiction.
- Expressed optimism that a threshold level “will eventually be identified.”
- Recognized that “developing practical, scientifically supported recommendations about nicotine levels in tobacco products involves filling gaps in knowledge in diverse areas...”

Where Did 0.3, 0.4, or 0.5 Originate?

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JACK E. HENNINGFIELD, Ph.D.

THE NEW ENGLAND
JOURNAL OF MEDICINE



ESTABLISHING A NICOTINE THRESHOLD FOR ADDICTION

most smokers is well established.⁴ Once a person is addicted to nicotine, quitting smoking is difficult, and more than 90 percent of the smokers who try to quit

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“an absolute limit of 0.4 to 0.5 mg of nicotine per cigarette should be adequate to prevent or limit the development of addiction in most young people”

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cigarette should be conceived not as a product but as a package. The product is nicotine. . . . Smoke is beyond question the most optimized vehicle of nicotine and the cigarette the most optimized dispenser of

IS THERE A THRESHOLD LEVEL OF NICOTINE INTAKE ASSOCIATED WITH ADDICTION?

We define addiction according to the Surgeon General's 1989 Report on Nicotine Addiction: it is the

Where Did 0.3, 0.4, or 0.5 Originate?

- Based analysis on work by Shiffman 1989 & 1990
- Assumed “chippers” are not addicted thus implicitly assumed a threshold of addiction
- Normalized biomarkers of exposure of chippers (5 mg nicotine/day) to a daily measurement for daily cigarette smokers
- Assumed 30 cigarettes per day
- Assumed 40% “bioavailability” (yield)

$$\frac{5 \text{ mg nicotine}}{\text{day}} \times \frac{\text{day}}{30 \text{ cigarettes}} \div 40\% \text{ yield} = \frac{0.42 \text{ mg nicotine}}{\text{cigarette}}$$

$$\frac{0.42 \text{ mg nicotine}}{\text{cigarette}} \times \frac{1 \text{ cigarette}}{0.7 \text{ g tobacco}} = \frac{0.6 \text{ mg nicotine}}{\text{g tobacco}}$$

A More Realistic Calculation

- Accept the chipper hypothesis at face value
- 14.1 cigarettes per day on average (MMWR, 2016)
- 20% nicotine yield – HCI (Ding et al., 2017)

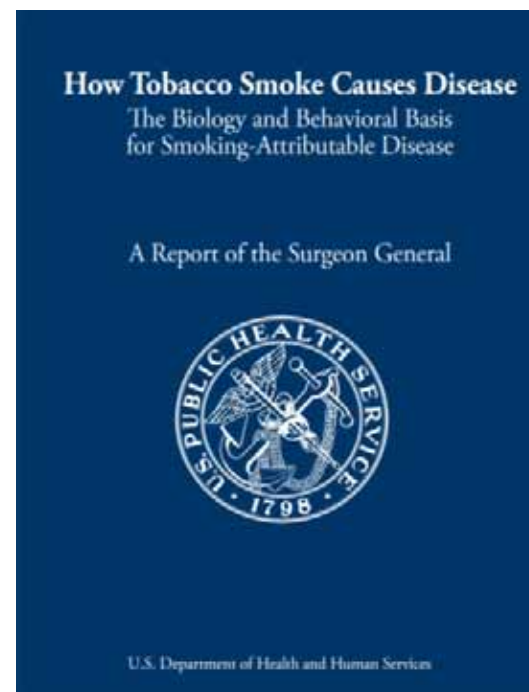
$$\frac{5 \text{ mg nicotine}}{\text{day}} \times \frac{\text{day}}{14.1 \text{ cigarettes}} \div 20\% \text{ yield} = \frac{1.78 \text{ mg nicotine}}{\text{cigarette}}$$

$$\frac{1.78 \text{ mg nicotine}}{\text{cigarette}} \times \frac{1 \text{ cigarette}}{0.7 \text{ g tobacco}} = \frac{2.5 \text{ mg nicotine}}{\text{g tobacco}}$$

There Are No Consensus Criteria for Diagnosing Nicotine Addiction

- Surgeon General (2010)
 - “The crux of understanding the pathophysiology of tobacco addiction and its measurement ... continues to evolve, and significant gaps in research are evident.”
 - “There is no established consensus on criteria for diagnosing nicotine addiction”

Source: Centers for Disease Control & Prevention, *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General* (2010)



ANPRM Treats Donny et al. as the Pivotal Study on VLNC Cigarettes

- Authors' Conclusions:
 - "In this 6-week study, participants assigned to cigarettes with 2.4 mg of nicotine or less per gram smoked 23 – 30% fewer cigarettes per day at week 6 than did participants assigned to cigarettes with 15.8 mg per gram."
 - "The cigarettes with the lowest nicotine content (0.4 mg per gram) reduced dependence according to both measures used in this study."



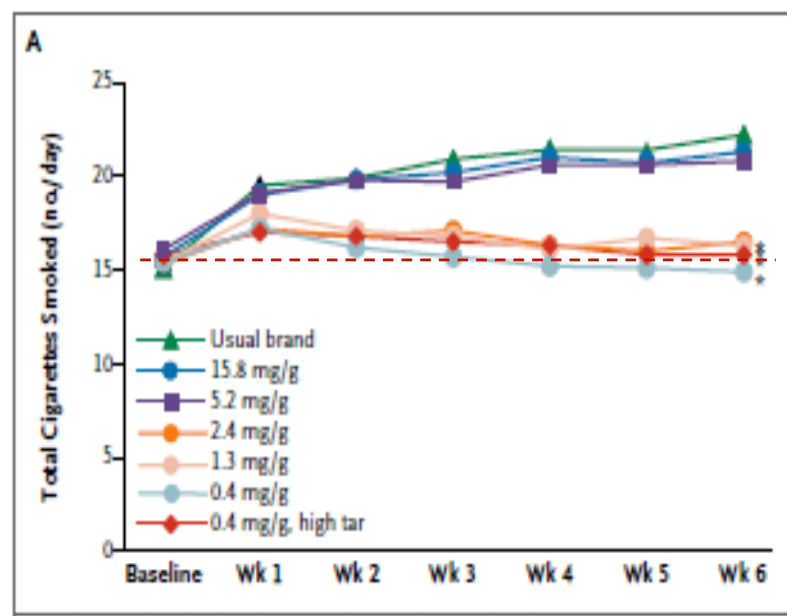
How the ANPRM cites Donny et al. (2015)

- “During the sixth week of the study, the average number of cigarettes smoked per day was lower for participants randomly assigned to cigarettes containing 2.4, 1.3 or 0.4 mg of nicotine per gram of tobacco ... than for those assigned to their usual cigarette brand or those cigarettes containing 5.2 or 15.8 mg/gram ...”
- “Those participants using cigarettes with the lowest nicotine content (0.4 mg per gram nicotine/gram of tobacco filler), demonstrated reduced dependence, and use of reduced nicotine cigarettes, including the VLNC cigarettes, with minimal evidence of withdrawal-related discomfort or safety concerns.”

Important Caveats

- One primary outcome – Cigarettes per Day at week 6
- According to protocol, study is sufficiently powered to detect differences in cotinine, FTND and withdrawal – based on results from Hatsukami 2010
- All comparisons made in relation to test cigarettes NOT participants' own brand (except CPD).
- QSU was administered in relation to the research cigarettes instead of the participants' own brand (e.g., craving for test cigarette).
- Nardone (2016) reported a 78% incidence of noncompliance

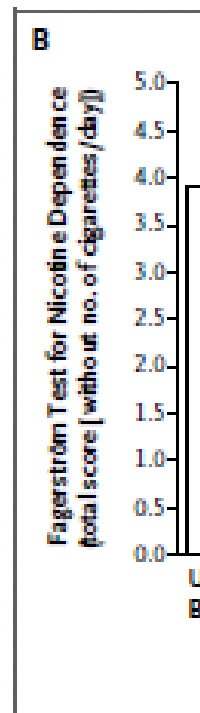
There Are No Differences Between Any Nicotine Content Groups and Baseline in CPD



Source: Donny et al. 2015

A Closer Look At Dependence Measures

- The authors report a “significant” difference between the lowest nicotine delivery cigarettes and the higher models.
- They do NOT assign any clinical relevance to these statistical differences.
- “[c]hanges of about 0.5 units in the [FTND] would not be expected to have any clinical importance for cessation.”



Source: Donny et

Perspectives

OPEN ACCESS

Cigarette prohibition and the need for more prior testing of the WHO TobReg's global nicotine-reduction strategy

Lynn T Kozlowski

WHO STUDY GROUP ON TOBACCO PRODUCT REGULATION (TOBREG) ADVISORY NOTE RECOMMENDS GLOBAL NICOTINE-REDUCTION STRATEGY

One can expect that the WHO Framework Convention on Tobacco Control (FCTC) Conference of the Parties may well be influenced by the recent WHO Tobacco Advisory Note¹ that supports, along with a host of others, recommendations to implement product regulations requiring reduction of nicotine levels in cigarettes.²⁻⁴ Note that these cigarettes are not the same as conventional lower yield cigarettes that were subject to complementary smoking that maintained tar and nicotine exposures to smokers.⁵ To quote from the report's conclusions, the first two 'regulatory recommendations' are:

- ▶ Mandated reductions in nicotine to minimally addictive levels should be supported by comprehensive regulation of all nicotine- and tobacco-containing products.
- ▶ Mandated reductions in nicotine to minimally addictive levels must be part of comprehensive tobacco control, including increased taxes on cigarettes, comprehensive smoking bans, anti-smoking educational campaigns and graphic warning labels on plain packaging (ref. 1, p. 24).

The next four regulatory recommendations concern precautions related to how to do this in the context of comprehensive tobacco control. The Advisory Note and its conclusions clearly appreciate and assume that (1) the nicotine-reduced cigarette will be challenging to traditional smokers and (2) alternative sources of nicotine are likely to be created, used and misused. The last recommendation warns: 'A strategy to reduce the addictiveness of tobacco is not recommended in the absence of developed capacity for market surveillance and product testing' (ref. 1, p. 29).

RESEARCH TO DATE

The recent, high-profile, randomized controlled trial is arguably the most substantial study until now and has been viewed as supportive, but one should look at it closely and critically.⁶ The report's introduction summarizes the prior literature: The results of several relatively small studies suggest (emphasis added) that cigarettes with very low nicotine content are associated with a desirable set of outcomes... (p. 1341). The article itself concludes: 'This study provides preliminary observational data suggesting (emphasis added) that as compared with the nicotine content of conventional cigarettes, a substantial reduction in nicotine content is associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events' (p. 1349). The clinical significance of any of the statistically notable effects ranges from unclear to doubtful. For example, changes of about 0.5 units in the Fagerström Test for Nicotine Dependence (FTND)⁷ would not be expected to have any clinical importance for cessation.⁸ The study was not designed to assess smoking cessation or the efficacy of use of alternative nicotine sources (as has been recognized as an overall component of the strategy).

The authors acknowledge that their sample was not representative of smokers in the USA, in part from excluding individuals with serious physical or mental disorders or who used any illicit drugs (except marijuana). Individuals with mental illness are more likely to be smokers, be more nicotine dependent and have a harder time quitting than the individuals assessed for 40-50% of the cigarettes consumed, despite being only 20% of the population.⁹⁻¹¹ Analyses of more representative US data find that mental illness was associated with a much greater likelihood of nicotine withdrawal and estimate that 48% of nicotine withdrawal syndrome diagnoses are attributable to mental illness.¹² It is, of course, not surprising or inappropriate that preliminary research would focus on healthy samples initially. However, given the recognized health disparities in smokers and the connections between smoking, mental illness, and use of alcohol and other substances, it should be important to assess the effects on such groups of restrictions to only very low-nicotine cigarettes, before recommending governmental regulations for all.

The authors note that 'use of non-study cigarettes was common', and explicitly acceptable, though discouraged, but also indicated as happening more often when one reduced-nicotine cigarettes. The up to US\$432 payment for participation was structured so that if one dropped out after something, one received only US\$25, with increasing awards for each type of session based on length. By completing all sessions and being timely, participants received a US\$200 bonus (making the maximum payment US\$432). Free cigarettes can be seen as an added financial incentive. Such an incrementally rewarded (a standard practice), secondary, 6-week opportunity for healthy volunteers to try low-nicotine cigarettes does not really simulate what would happen if a representative

Model	Tar Content (mg/g High Tar, approx.)
U (Ultra)	0.35
B (Bull)	0.4

Linked

- <https://doi.org/10.1136/tobacco.2016-021350>
- <https://doi.org/10.1136/tobacco.2016-021354>

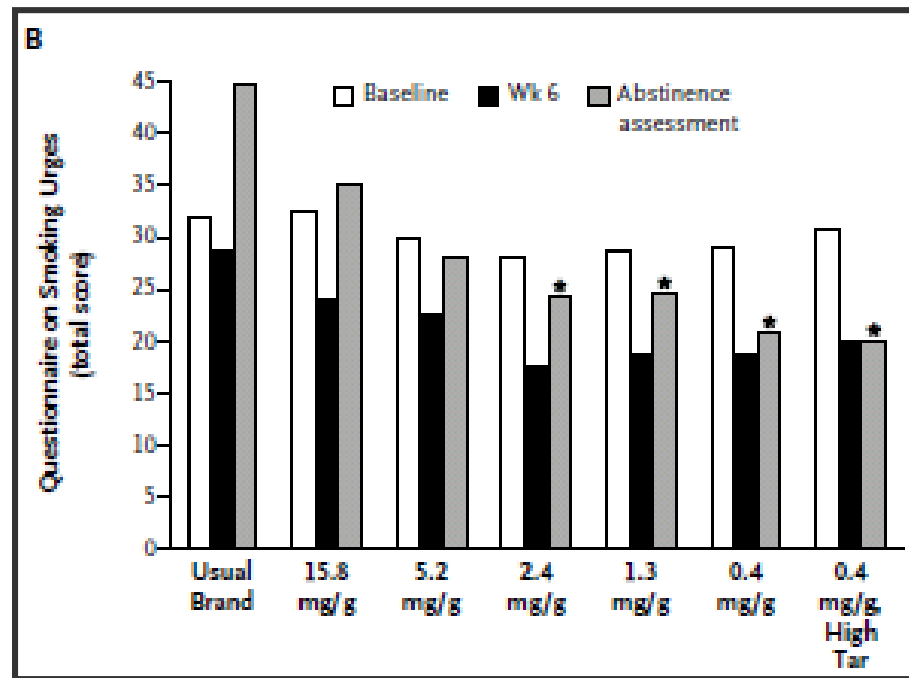
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To cite: Kozlowski LT, Bob Carter 2017, *BMJ* 354:g1-4.

BMJ

Kozlowski LT, Bob Carter 2017, *BMJ* 354:g1-4. doi:10.1136/bmj-2016-02095

A Closer Look At Withdrawal Measures

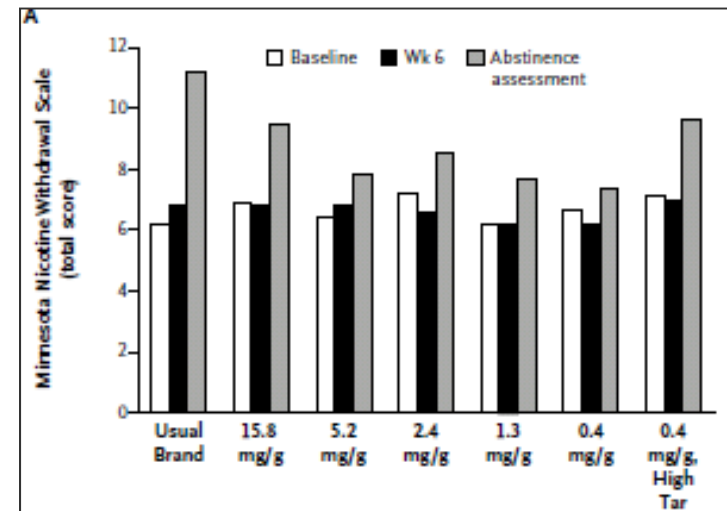
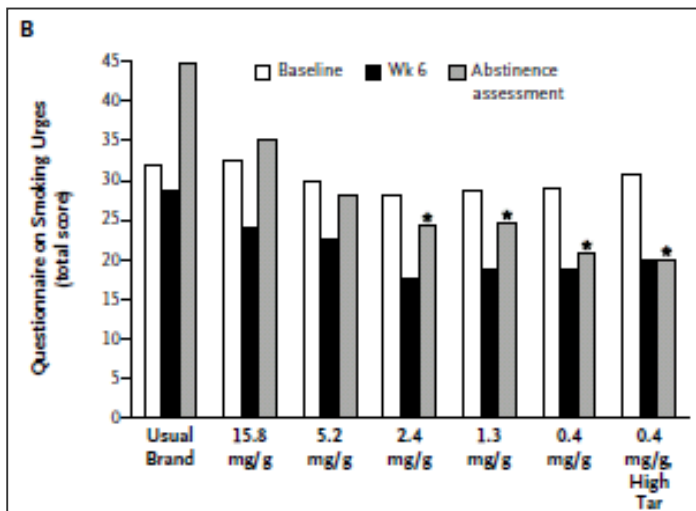


Source: Donny et al. 2015.

- QSU administered in relation to 15.8 mg nicotine/g research cigarette NOT Usual Brand
- Every single SPECTRUM® model is significantly different from participants' own brand

A Closer Look At Withdrawal Measures

- Typically, the QSU and MNWS co-vary
- No differences in MNWS were observed between research cigarettes



Source: Donny et al. 2015

Analysis of Recent VLNC Cigarette Literature

- This analysis demonstrates that, in most measures, across multiple studies 2.4 mg/g is not different than 0.4 mg/g.

Source: ALCS Comments to FDA's ANPRM on Nicotine

Study	Measure	Area	Nicotine content (mg/g)				
			NRC102	NRC200	NRC300	NRC400	NRC500
			0.4	1.3	2.4	5.2	15.8
Donny 2015	Total CPD at week 8	CPD					
Donny 2015	Total CPD at week 8 - menthol	CPD					
Donny 2016	Total CPD at week 8 - non-menthol	CPD					
Donny 2015	Study Qq CPD at week 8	CPD					
Donny 2015	Nonstudy cig use						
Donny 2015	Quit attempt 30 day follow-up	Quit					
Donny 2015	CPD 30 day follow-up	CPD					
Donny 2015	Urinary total NE	Exposure					
Donny 2015	Urinary tHAA	Exposure					
Donny 2015	Expired CO at week 8	Exposure					
Donny 2015	CO boost after 1 cigarette	Exposure					
Donny 2015	Total puff volume	Topography					
Donny 2015	Perceived nicotine level	Subjective					
Donny 2015	CPD @ \$5/pack	Behavior					
Donny 2015	WISDM - week 8	Dependence					
Donny 2015	Fagerstrom - week 8	Dependence					
Donny 2015	MMWS - week 8 (total & max)	Dependence					
Donny 2015	GSU (total)-w k8	Dependence					
Donny 2015	GSU (total)-w k8 - abstinence	Dependence					
Donny 2015	GSU (Factor 1)-w k8 - abstinence	Dependence					
Donny 2015	GSU (Factor 2)-w k8 - abstinence	Dependence					
Smith 2017	Estimated CPD @ \$4. \$10/pack	Behavior					
Smith 2017	Estimated CPD @ \$20/pack	Behavior					
Smith 2017	Smoke 0 CPD @ >\$0/pack	Behavior					
Smith 2017	Quit in 1 year if only product option	Behavior					
Smith 2017	Qmax (max \$/day w/ spend)	Behavior					
Smith 2017	Intensity (QDP # free)	Behavior					
Smith 2017	Breakpoint (lowest price to 0 CPD)	Behavior					
Smith 2017	Breakpoint after 24h abstinence	Behavior					
Rupperecht	Weight gain-wk6, compliant	Weight					
Perkins 2016	Nicotine discrimination (Smokers)	Threshold					
Perkins 2017	Nicotine discrimination (S vs T5)	Threshold					
Perkins 2017a	Nicotine discrimination - Menthol	Threshold					
Perkins 2017a	Nicotine discrimination - Non-	Threshold					
Higgins 2017	MMWS (Total)	Dependence					
Higgins 2017	MMWS (Desire)	Dependence					
Higgins 2017	GSU (Factor 1)	Dependence					
Higgins 2017	GSU (Factor 2)	Dependence					
Higgins 2017	Breakpoint	Behavior					
Higgins 2017	Direct test of preference	Behavior					
Faulkner 2017	Craving and w/ withdrawal reduction	Dependence					
Faulkner 2017	Positive or negative affect	Dependence					
Faulkner 2017	Sustained attention	Performance					
Faulkner 2017	Liking	Dependence					

Altria Client Services | Donna Smith | September 17, 2018 | Final | TSRC 2018 | 17



Comments to the ANPRM Docket from Donny

- “Available data suggest that nicotine should be reduced to a maximum of 2.4 mg/g and that there are likely to be additional benefits to decreasing content to ≤ 0.4 mg/g.”
- “Similarly, although most smokers cannot discriminate between cigarettes with 2.4 and 0.4 mg/g, some can, suggesting that reducing nicotine content to ≤ 0.4 mg/g may impact more smokers.”
- “Reducing nicotine content to ≤ 0.4 mg/g of tobacco will likely maximize the net benefits to the population”
- “These data suggest additional benefits to public health for establishing a standard of ≤ 0.4 mg/g”
- “To minimize the likelihood of compensation...FDA should reduce nicotine as low as possible”

Dr. Eric Donny

Professor

Department of Physiology & Pharmacology

Social Science & Health Policy

Wake Forest School of Medicine

Comments to FDA's ANPRM on Nicotine, July 13, 2018



FDA Minimizes Unintended Consequences

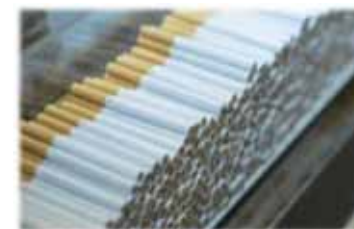
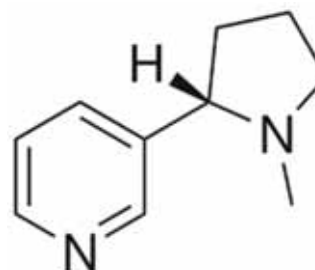
- Compensation

- “According to studies involving very low nicotine cigarettes ... researchers expect there would be little or no compensatory smoking.”

Source: Fed. Reg. Vol 83, No. 52/11829

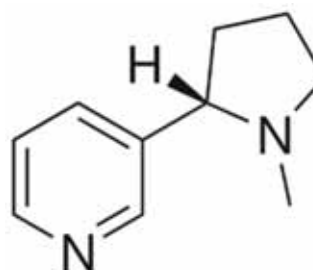
- “FDA expects ... the nicotine level in cigarettes would be self-limiting (e.g., smokers would be unable to obtain their nicotine dose from cigarettes no matter how they smoke them) and eventually would stop trying to do so, making it easier for smokers to make more successful quit attempts...”

Source: Fed. Reg. Vol 83, No. 52/11824



FDA Minimizes Unintended Consequences

- Consumer Impact
 - Will consumers believe VLNC cigarettes are safer?
 - What are the consequences of withdrawal effects on a population level?



Best Available Science?

- Studies referenced in ANPRM are from a small group of researchers and none involve a nationally representative cohort of smokers
- Significant scientific gaps exist within these studies
- Full data sets and original protocols are unavailable to date
- No access to research cigarettes
- Dozens of clinical studies are currently being conducted

On What Science Should the Agency Rely?

- Weight of Evidence analysis of well-conducted studies by multiple stakeholders
- Analyses in real-world conditions
 - Illicit products
 - Availability of sensorially acceptable VLNC products
 - Long term effects
 - Nationally representative
- Studies using the continuum of risk and FDA framework in their design

Policy On Which Everyone Can Agree

THOMAS J. MILLER
Attorney General



IOWA DEPARTMENT OF JUSTICE
OFFICE OF THE ATTORNEY GENERAL

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July 11, 2018

Food and Drug Administration
21 CFR Part 1330
Docket No. FDA-2017-N-6189
Advance notice of proposed rulemaking
Tobacco Product Standard for Nicotine Level of Combusted Cigarettes

We are responding to the request for comment on the advanced notice of proposed rulemaking (ANPRM) for a tobacco product standard for the nicotine level in combusted cigarettes. We welcome the opportunity to provide advice at this stage.

In the professional public health community, there is a wide range of views on the merits, practical viability, and likely consequences of introducing a rule to reduce nicotine levels in cigarettes, and possibly in other combustible tobacco products. Views range through a spectrum embracing:

1. Full enforcement for a rapid implementation of a tobacco product standard to reduce the nicotine level in cigarettes and in other combustible tobacco products;
2. A sequential approach, in which the full potential of alternative nicotine delivery systems is realized to prepare the ground first, and then a nicotine standard follows;
3. A nicotine standard should be held in reserve as an "agency threat" to force the pace of reform in the tobacco/nicotine marketplace;
4. A nicotine standard would be impractical and ultimately unnecessary, and a diversion from taking other more realistic measures;
5. A nicotine standard would be excessively coercive and based on a poor legal and political mandate. It would cause an active black market and have other unintended consequences.

It is not our purpose in this comment to resolve this debate over the appropriate strategy for a nicotine standard and we may individually take different positions on it. However, we all agree that there is one important requirement common to each of the perspectives above: that is the availability of low-risk non-combustible alternative tobacco or nicotine products that are sufficiently satisfying alternatives to cigarettes that smokers who choose to continue to use nicotine would be willing to switch to them.

The availability of alternative nicotine delivery systems (ANDS) is integral to a strategy of reducing nicotine levels in cigarettes by providing beneficial migration pathways for continuing nicotine users (i.e. 2 above); necessary to mitigate a credible threat to introduce such a rule (3 above); and required as an alternative strategy which renders a reduced nicotine rule for cigarettes unnecessary

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- Letter from the AG of Iowa in response to the nicotine ANPRM
- Signed by the AG and 17 Public Health scientists – including Eric Donny
- Comments focus on the availability of alternative nicotine-containing products as a more appropriate means of achieving public health goals