Should FDA try to move smokers to e-cigarettes or other less harmful tobacco-nicotine products and, if so, how?

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FDA's Embrace of the Continuum of Harm

- July 28, 2017 Speech by Dr. Gottlieb:
  - "[W]e must acknowledge that there's a continuum of risk for nicotine delivery."
  - "Looking at ways to reduce nicotine levels in cigarettes so that they are minimally or non-addictive, while not altering the nicotine content of noncombustible products such as e-cigarettes, is a cornerstone of our new and more comprehensive approach to effective tobacco regulation."

Mitch Zeller's Prior Articulation of the Continuum

- 2013 - "Along the path of the continuum of risk are products that pose less harm to the individual than cigarettes but for which less is known about their population-level health impacts. Here, we would place smokeless and dissolvable tobacco products as well as the 'e-cigarette'."
- 2015 – FDLI – two slides from Mitch Zeller's presentation:

FDA'S REGULATION OF TOBACCO: A YEAR IN REVIEW

CENTER FOR TOBACCO PRODUCTS

Presented by
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Center Director
FDA Center for Tobacco Products

October 21, 2015

Looking at nicotine differently

- Recognize that there is a continuum of nicotine-containing products
- Understand that people smoke for the nicotine but die from the tar
- Acknowledge public health opportunity
- Also acknowledge role that flavored tobacco products may play in holding back progress in harm reduction

The nicotine reality

- It's not the drug…it's the delivery mechanism
- The disease and death is primarily due to combusting tobacco products
- So if Michael Russell was right 40 years ago, how should we be thinking about nicotine today?
- The "net" assessment of population-level impact is key
  - Potential benefit to currently addicted smokers unable or unwilling to quit who completely substitute
  - Clear harm from any initiation by kids
  - Unknown longer-term impact of dual use rather than complete substitution
  - Unknown impact on cessation rates

Public Health Consensus No. 1 – ENDS Appear to be Less Toxic than Combustion Cigarettes Based on Laboratory Analyses

- Broad agreement, across public health spectrum (including ENDS skeptics), that ENDS products deliver significantly fewer toxicants to the user than combustion cigarettes.
  - Stan Glantz – referring to the "widely-accepted fact that e-cigarettes deliver lower levels of most cancer-causing chemicals" https://tobacco.ucsf.edu/evidence-e-cigs-increase-cardiovascular-risk-keeps-piling-effects-heart-rhythm-and-oxidative-stress-1)(2/15/17
  - Though no agreement on precise amount of reduced risk:
    - Stan Glantz - ""I think ecigs are about 30-50% as dangerous as cigarettes"
    - Public Health England – "best estimates show e-cigarettes are 95% less harmful to your health than normal cigarettes "

First Long-Term Study on ENDS Use – Corroborative of PH Consensus of Reduced Toxicity

- Nicotine, Carcinogen, and Toxin Exposure in Long-Term E-Cigarette and Nicotine Replacement Therapy Users - A Cross-sectional Study Annals of Internal Medicine (2/2017)
  - the authors analyzed urine and saliva samples from five groups of study participants (smokers only, former smokers with long-term e-cigarette use only, former smokers with long-term NRT use only, long-term dual users of cigarettes and e-cigarettes, and long-term dual users of cigarettes and NRT) for biomarkers of tobacco specific nitrosamines (TSNA's) and volatile organic compounds (VOC's) involved with cancer, cardiovascular and pulmonary diseases.
  - The e-cigarette-only and NRT-only users had "significantly lower" metabolite levels for TSNA's and VOC's then the other three groups and e-cigarette-only group had lower metabolite levels than NRT-only group.

Public Health Consensus No. 2 – At the Individual Level, it is Beneficial for the Current Adult Smoker who Cannot or Will Not Quit to Completely Switch to an ENDS Product

- CDC - "E-cigarettes have the potential to benefit adult smokers who are not pregnant if used as a complete substitute for regular cigarettes and other smoked tobacco products." https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm
- Stan Glantz – "If a patient has failed initial treatment, has been intolerant of or refuses to use conventional smoking cessation medication, and wishes to use e-cigarettes to aid quitting, it is reasonable to support the attempt."
- AHA Policy Statement - "If a patient has failed initial treatment, has been intolerant to or refuses to use conventional smoking cessation medication, and wishes to use e-cigarettes to aid quitting, it is reasonable to support the attempt."
- WHO Report - "In considering ENDS as a potential cessation aid, smokers should first be encouraged to quit smoking and nicotine addiction using a combination of already approved treatments. However, at the individual level, experts suggest that in some smokers who have failed treatment, have been intolerant to it or who refuse to use conventional smoking cessation medication, the use of appropriately-regulated ENDS may have a role to play in supporting attempts to quit."

Where Do We Not Have a U.S. Public Health Consensus?

- Flavors (though perhaps a consensus on the measuring stick – appropriate if shown to be promotive of adult switching without attracting non-smoking youth)
- Youth (except that there is a consensus that non-smoking youth should not initiate the use of any nicotine-containing product)
- Gateway (though a recognition that a true showing of gateway would create a significant public health concern)
- Dual use (though likely an acceptance that a transitional period of dual use on the way to complete switching would be acceptable)
- Precise magnitude of risk reduction

What Do Current Adult Smokers Think on the Two Issues of PH Consensus?

- There has been a decline in the belief in the reduced risk associated with ENDS - less than 50% of current adult smokers now believe that ENDS present less risk than combustion smoking.
- Not surprising –
  - Numerous frightening headlines regarding anti-freeze in e-liquid, high levels of formaldehyde in the aerosol, popcorn lung risk, exploding batteries, etc.
  - Absence of clear message on PH Consensus items 1 and 2 by FDA, doctors, etc.
- The average individual has no real basis to independently make sense of this controversy
- At the same time – as reported by the CDC, ENDS have emerged as the number one U.S. quit aid (Quit Methods Used by US Adult Cigarette Smokers, 2014–2016) (4/17) and are now seen as contributing to a historic rise in the national smoking cessation rate (Zhu, et al., E-cigarette use and associated changes in population smoking cessation: evidence from US current population surveys) (7/17)

What is the Size of the Public Health Prize

- “Potential deaths averted in USA by replacing cigarettes with e-cigarettes” (Levy, et al) (Tobacco Control) (10/17)
- Models the potential life-saving benefits over a 10 year period, on a population level, from large-scale switching of smokers to electronic nicotine products/ENDS.
- Optimistic (PHE) Scenario - 6.6 million fewer premature deaths and 86.7 million fewer life years lost.
- Pessimistic (Glantz) Scenario - 1.6 million fewer premature deaths and 20.8 million fewer life years lost.
- “Information dissemination policies that provide the best available information on the relative risks of e-cigarettes are likely to encourage switching to e-cigarette use.”

FDA Has Two Fundamental Public Messaging Alternatives

- Do nothing/status quo - leave smokers in the dark on relative risk and the apparent benefits of complete switching until an ENDS company navigates the MRTP (not PMTA) pathway, which presumably won't happen for years
- Begin a national media campaign, now, to educate adult smokers about the continuum of harm and about the likely health benefits of complete switching for the adult smoker who cannot/will not quit.

FDA Action No. 1 – FDA Should Issue a Clear Statement to Adult Smokers and Medical Professionals that is Consistent with the US PH Consensus

- Key elements
  - Smokers should quit smoking
  - If they need assistance they should use an FDA-approved cessation product/therapy
  - If they cannot or will not quit, they are making a positive health choice, based on currently available science and data, by switching completely from combustion smoking to ENDS use
  - No need to take a position on non-consensus issues (flavors, gateway, youth, magnitude of harm reduction)
  - Will need to periodically update as more data becomes available
  - Should be national and of a size and scope equivalent to other FDA campaigns related to smoking

FDA Is Already Engaged in National Public Health Advertising Campaigns Around Smoking to Change Attitudes and Influence Behavior

The Real Cost

- Description - "The Real Cost" campaign launched nationally in February 2014 across multiple media platforms including TV, radio, print, web, social media, and out-of-home sites, like billboards. Initial campaign advertising focused on reaching the nearly 10 million youth ages 12-17 in the United States who are either open to trying smoking or are already experimenting with cigarettes."
- ENDS Expansion – Expanded in August 2017 to "discourag[e] the use of e-cigarettes and other electronic nicotine delivery systems (ENDS) by kids."
- Goal – "The goal is to prevent youth who are open to tobacco from trying it and to reduce the number of youth who move from experimenting with tobacco to regular use." Influence "tobacco-related risk perceptions and beliefs."

Positively Influencing “tobacco-related risk perceptions and beliefs”

This Real Life

- Description - The campaign launched in May 2016 and has a national presence online through FDA's social media and the campaign website. The paid advertising efforts (print, digital, and out-of-home) focus on existing LGBT media that reaches a high percentage of the target audience in 12 markets throughout the United States"
- Goal – "FDA will conduct a rigorous, multi-year outcome evaluation designed to measure the campaign's effectiveness in changing tobacco-related attitudes, knowledge, and beliefs."

Fresh Empire

- Description - the FDA's public education campaign designed to prevent and reduce tobacco use among at-risk multicultural youth ages 12–17, specifically African American, Hispanic, and Asian American/Pacific Islander youth. In October 2015, the FDA expanded the Fresh Empire campaign to approximately 37 markets with TV, print, and digital advertising. Fresh Empire also rolled out its localized efforts, including out-of-home and radio ads, and local events in more than 25 markets.
- Goal – "The FDA expects the Fresh Empire campaign to affect positive changes in knowledge, attitudes, and beliefs within 24 months among multicultural youth ages 12–17 who are open to smoking or are already experimenting with cigarettes."

Current FDA/CTP Public Health Messaging on ENDS Battery Risks

CENTER FOR TOBACCO PRODUCTS

5 TIPS TO HELP AVOID "VAPE" BATTERY EXPLOSIONS

1. Consider using vape devices with safety features

such as firing button locks, vent holes, and protection against overcharging.

2. Keep loose batteries in a case to prevent contact with metal objects.

Don't let batteries come in contact with coins, keys, or other metals in your pocket.

3. Never charge your vape device with a phone ortablet charger.

Always use the charger that came with it.

4. Don't charge your vape device overnight

or leave it charging unattended.

5. Replace the batteries if they get damaged or wet.

If your vape device gets damaged and the batteries are not replaceable, contact the manufacturer.

FDA IS AWARE OF EXPLOSION EVENTS AND IS COLLECTING DATA TO ADDRESS THIS PROBLEM.
Report to FDA at www.safetyreporting.hhs.gov

For a complete list of references, go to **www.fda.gov/tobacco** and search for **"tips to help avoid vape battery explosions."**

www.fda.gov/tobacco @FDATobacco facebook.com/fda

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FDA Action No. 2 – Enabling Responsible Innovation of Non-Combustible Products Through Product Standards

- "[W]e must recognize the potential for innovation to lead to less harmful products, which, under FDA's oversight, could be part of a solution." (Scott Gottlieb, 7/28/17)
- Legal basis for product standards - FDA may adopt a tobacco product standard if it finds that the standard is "appropriate for the protection of public health." 21 U.S.C. § 387g(a)(3)(A)
- Tobacco product standards can include: (1) requirements relating to composition, properties, or labeling; (2) standards setting levels of nicotine yields or lessening or eliminating the presence of other constituents; (3) standards governing the construction, components, ingredients, additives, constituents, and properties of the product; and (4) requirements for testing, sale and distribution, and labeling necessary to assure the proper use of the product. 21 U.S.C. § 907(a)(4).

Proposed Approach to Standards

- ENDS product standards (which may be periodically updated as appropriate for the protection of public health) should include requirements regarding:
  - Ingredients, both acceptable (propylene glycol and/or glycerin as excipients, etc.) and unacceptable (e.g., diacetyl);
  - Device components and performance (e.g., maximum temperature limits, standard safety features such as short-circuit protections, battery and charger specifications); and
  - HPHC exposure limits (as measured based on established standardized methodologies and informed by the current toxicological science).
- Need to balance safety promotion with enablement of responsible innovation
- Significance of Standards Compliance - certification of compliance with applicable product standards can be included in a PMTA and/or MRTP in lieu of non-clinical/human subject and population level studies – would remove most burdensome aspects of PMTA/MRTP and promote/speed innovation of reduced harm products while providing appropriate safeguards for consumers.

Comments on the Reduced Nicotine Concept

- We are supportive of FDA's comprehensive approach
- However – mindful of CTP's experience with menthol and FDA's own recognition that important questions remain regarding VLNC's – there is a practical reality that this change is not imminent and may not happen for years, if ever
- FDA actions on non-combustible products can happen in the very near term (especially with respect to public messaging) and can help smokers almost immediately – these should not be held up while the VLNC issue is fully-sorted and possibly implemented