The Future of Nicotine Products and FDA's Nicotine Steering Committee

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November 2017 – Announcement of New Steps and a Public Meeting to Promote NRT Innovation

- CSU retail sales or shipments, especially information about the type of CSUs sold and the number of units sold in recent years;
- the number of CSUs in use;
- studies, tests, or descriptions of technologies or design changes that address tip-over injuries and estimates of costs associated with those features, including manufacturing costs and wholesale prices;
- the expected impact of technologies or design changes that address tip-over injuries on manufacturing costs or wholesale prices;
- the potential impact of design changes to address CSU stability on consumer utility; and
- information about whether any stability requirements for CSUs in ether a voluntary standard or potential mandatory rule could have a disparate impact on small entities, such as small manufacturers or importers.

In addition, the Commission invites interested parties to submit any existing standards, or portions of them, for consideration as a consumer product safety standard. The Commission also invites interested persons to submit a

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 15

[Docket No. FDA–2017–N–6529]

The Food and Drug Administration's Approach To Evaluating Nicotine Replacement Therapies; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing a public hearing on FDA's approach to evaluating the safety and efficacy of nicotine replacement therapy (NRT) products, including how they should be used and labeled.

DATES: The public hearing will be held on Friday, January 26, 2018, from 9 a.m. to 5 p.m. The public hearing may be extended or may end early depending on the level of public participation. Persons seeking to attend or to present

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://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 *https://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 (see "Written/Paper

The Nicotine Steering Committee

- Charged with re-evaluating and modernizing FDA's approach to development and regulation of NRT

- Highlighted Possibilities:
  - Labelling and indication changes for existing NRT
  - New products with different delivery rates or mechanisms
  - New clinical trial endpoints

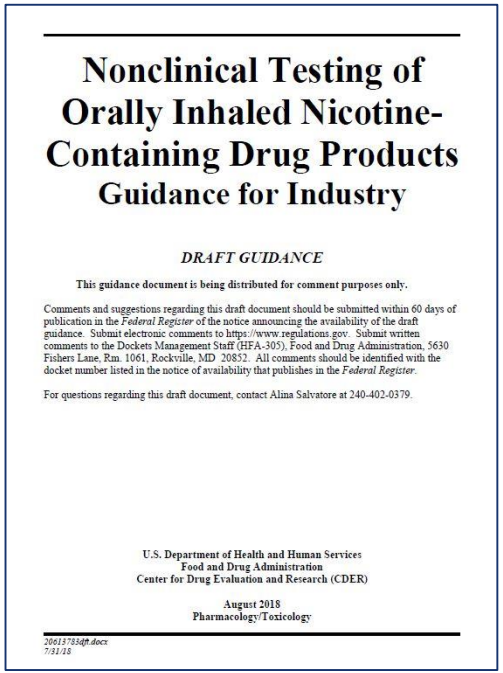
The Nicotine Steering Committee

"If there are new kinds of NRTs — with different characteristics or routes of delivery – that can offer additional opportunities for smokers to quit combustible tobacco, we want to explore what steps we can take using our own regulatory policies to enable these opportunities, while making sure these products are demonstrated to be safe and effective for their intended use."

January 26, 2018 Public Hearing – FDA Approach to Evaluating Nicotine Replacement Therapies

- More and Better NRT Products are Needed
- Improved Appeal/Satisfaction/Nicotine Delivery
- Expanded Indications
- Expanded Clinical Endpoints Reflective of the Real World
- MHRA-style Pharmacokinetic Bracketing
- No Need for IND Two-species Inhalation Toxicity
- Labelling Changes to Correct Nicotine Misperceptions

August 2018 – Draft Guidance for Nonclinical Testing



Nonclinical Testing of Orally Inhaled Nicotine-Containing Drug Products
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Alina Salvatore at 240-402-0379.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

August 2018
Pharmacology/Toxicology

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- Focus on novel components, chemicals, and impurities due to formulation or delivery system
- Allows for PK bracketing to bypass nonclinical testing of “nicotine alone”
- Still requires rodent and non-rodent inhalation toxicity studies

…but wait, there's more:

"While one significant focus will be on NRT, the mandate of this committee will be to address the FDA's overall approach to nicotine. It will create a forum for developing and implementing nicotine policy and regulation to address the public health crisis of tobacco usage in this country."

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Improving smoking cessation

Dorothy K. Hatsukami, PhD
University of Minnesota
Masonic Cancer Center

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Directions for nicotine replacement therapies

- Educate
  - Dispel misperceptions about nicotine
- Liberate
  - New labelling and indications for existing nicotine replacement therapies
- Innovate
  - Products that have more appeal and potentially greater abuse liability
- Expedite
  - More efficient, less onerous and costly approval process without compromising safety and efficacy

Educate

- There are significant misperceptions or lack of knowledge of harm of nicotine and NRT in smokers[1-4] and healthcare providers.[5-6]
- Misperceptions have been associated with reduced uptake and optimal use of NRT.[1]
- Reduced optimal NRT use results in less efficacy.

Reduced risk claims: "*Nicotine replacement therapy is substantially less harmful to health than cigarette smoking*"

Liberate: Expand labelling and Indications

- **Combination NRT medications**
  - Studies show that combination medications are safe and more effective than monotherapy.[7-8]
  - Recommendation for use of short-acting and long-acting medications have been made by:
    1. Cochrane report[9]
    2. The U.S. Department of Health and Human Services Clinical Practice Guideline for Tobacco Use and Dependence[10]
    3. National Comprehensive Cancer Network[11]

- **Long term use of NRT for smoking cessation**
  - Extended duration of NRT might increase quit rates and recovery from smoking relapse in some smokers.[7,9,10, 26]

- **Pre-quit NRT use**
  - Not all smokers are ready to quit smoking.
  - Almost half planning to quit in next 12 months were interested in gradual reduction.[12]
  - Reducing to quit with NRT is more effective than placebo.[7]
  - Reduce to quit results in comparable quit rates as abrupt cessation.[13]

Innovate: NRT with greater appeal and addiction potential to complete with cigarettes

- Compared to NRT, ENDS have greater appeal and lead to greater substitution for cigarettes[14-17] and, more recently, have exhibited greater uptake for the purposes of smoking cessation.[18]
- A few clinical trials and epidemiological studies have suggested that ENDS can be an effective smoking cessation tool,[19-21, 27,28] especially with frequent use,[22-25] yet major impediments for conducting such trials exist in the U.S.

Expedite

- Utilize existing research and/or recommendations made by credible organizations without needing costly trials.
- Consider population based data to help determine potential efficacy and safety.
- Utilize existing data to determine safety for the same class of drugs.
- Use continued smoking as a comparator.
- Do not require that a treatment be better than an existing treatment; efficacy can be comparable.
- Coordinate evidence-based information between CDER and CTP.

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Pinney Associates

Science. Strategy. Solutions.

We've seen this movie before – the Nicotine Steering Committee and development standards for novel nicotine-containing drugs

Joe G. Gitchell

26 October 2018

FDLI Tobacco and Nicotine Products Regulation and Policy Conference

Financial Disclosures

- I work for PinneyAssociates, a health consulting firm. PinneyAssociates provides consulting services on tobacco harm minimization (including nicotine replacement therapy and digital vapor products) to Niconovum USA, RJ Reynolds Vapor Company, and RAI Services Company, all subsidiaries of Reynolds American Inc. RAI was purchased by British American Tobacco in July 2017
- I also own an interest in intellectual property for a novel nicotine gum that has neither been developed nor commercialized

Overview

- Promise of comprehensive plan – greater reach
- To reform requires substantial rethinking regulating NCPs as drugs - nicotine's unique situation
- Long history of trying to do this

FDA's Comprehensive Approach

"This new regulatory step advances a comprehensive policy framework that we believe could help avoid millions of tobacco-related deaths across the country."

— Scott Gottlieb, M.D.

CENTER FOR TOBACCO PRODUCTS

VLNCs

+

NRTs/Rxs

NNPs

Prospects for meaningful change

- "…new steps to foster innovation in nicotine delivery, where such innovation could truly make a positive public health impact."
- "A key part of this plan also includes new efforts to enable medicinal nicotine products to play a more prominent role in helping smokers try to quit with help, to quit successfully, and to stay quit."
  - **HEALTHY INNOVATION, SAFER FAMILIES: FDA'S 2018 STRATEGIC POLICY ROADMAP**

Draft guidance on nonclinical testing requirements

- Outlines extensive requirements for products that are already being used by millions of humans
- Clinical testing guidance still to come, but not optimistic
- Big differences from UK MHRA's licensing requirements

A long road….

Conferences… Conference Proceedings… Workshops… Citizen Petitions… Workshops… Notice of Findings… Hearings… Dockets… Draft Guidances…

Why is this so hard to evolve CDER's approach?

- IDK first-hand, but have speculations
  - Fundamental regulatory incentives favor risk aversion
  - Concerns about precedent-setting
- If FDA does want medicinal products to play a more prominent role in helping smokers stop, they need to reform the development pathway substantially