THE OHIO STATE UNIVERSITY

Tobacco Regulation in a Changing Policy Landscape: Synthetic Nicotine

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University of Michigan Tobacco Research Network/CAsToR

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Denied FDA Authorization, Vaping Companies Start to Explore Loopholes

BY ALEX NORCIA AUGUST 30, 2021

HEALTH

Some Vaping Companies Are Turning to Synthetic Nicotine to Outsmart the FDA

Filter, 8/30/21; Time, 9/17/21

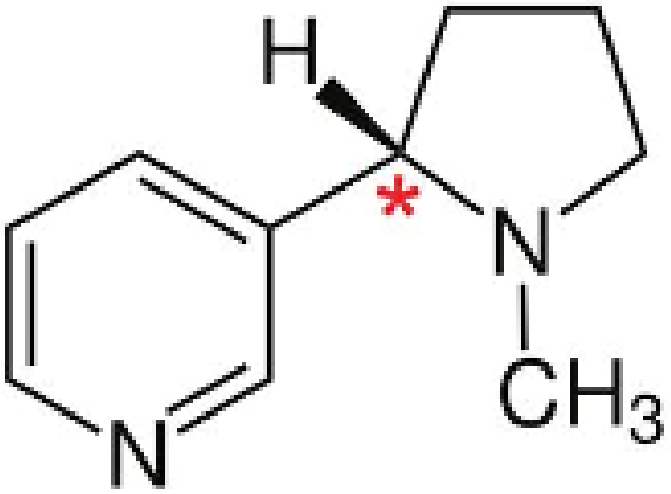
Chairman Krishnamoorthi Launches Investigation into the Production, Sale of Unregulated Synthetic Nicotine

Nov 8, 2021 | Press Release

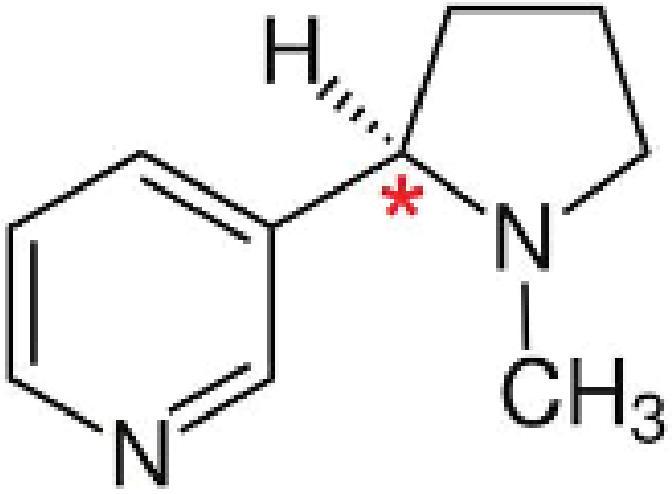
Requests Transcribed Interviews with Puff Bar Co-Chief Executive Officers

Washington, D.C. (November 8, 2021)—Today, Rep. Raja Krishnamoorthi, Chair of the Subcommittee on Economic and Consumer Policy, sent letters to two companies that manufacture or sell synthetic nicotine products, requesting information about the companies and their sale of these products, which are unregulated by the Food and Drug Administration (FDA). The Chairman sent a letter to Next Generation Labs LLC, which claims to be "the market leader" in the production and sale of synthetic nicotine. He also sent a letter to Puff Bar, the top children's e-cigarette brand, which claims to have reformulated its products with synthetic nicotine after it was found to be in violation of Food and Drug Administration (FDA) law.

Two Forms of Nicotine



S-nicotine



R-nicotine

Adapted from Jordt, *Tobacco Control* 2021

Synthetic Nicotine

- Until recently, nicotine used in commercial products was exclusively sourced from tobacco plants

- Processes for synthetizing nicotine from chemicals – without tobacco – have been known for >100 years, but were too expensive for commercial use

- Synthetically-derived methods produce a racemic mixture of R-nicotine and S-nicotine.
  - Little is known about by-products formed during production
  - Several recently patented methods allow for isolation of S-nicotine

Tobacco-Derived Nicotine	Synthetic Nicotine
• Extracted from tobacco plant • Consists predominantly (S)-form (>90%) with (R)-form presence below 5% • Contains known natural impurities such as anabasine, anatabine, nornicotine, myosmine, etc. • USD 60 to 300 per liter*	• Made from a mixture of chemicals • Consists of a mixture of (R,S)-nicotine in varying percentages • Contains varying levels of by-products, depending on the starting material used in the production • Unknown toxicity • USD 600 per liter*

**Nicotine concentration between 7 to 10% with propylene glycol or glycerol as base liquid.*
Cost varies, depending on the amount of nicotine in the formulation and quantity ordered.

Source: Adapted form N.P. Cheah

Producers


NextGenerationLabs


tfn
Nicotine
BEWARE OF THE FAKES


What is TFN®


CNT
NICOTINE IN ITS
PUREST FORM

Product/Type/Website	Claims
2One/nicotine pouch www.20nelabs.com	"We eliminated tobacco's unpleasant flavors and impurities by producing only high-quality, tobacco-free nicotine."
Pacha Mama/ disposable e-cigarette charlieschalkdust.com/pages/pacha mama-disposables	"Aims to help adult smokers take their first steps in going smokeless."
Nic-S/nicotine pouch nic-s.com	"A responsible product that is crafted with ingredients as clean as our Nordic air."
Outlaw Dip/oral snuff outlawdip.com	"Our dip is 100% tobacco free and we use pharmaceutical grade nicotine that does NOT come from tobacco."
NIIN/disposable e-cigarette and nicotine pouch niinpouches.com	"Completely free of the many residuals and constituent impurities that are commonly found in tobacco-derived nicotine."

WHAT DO NICOTINE POUCHES CONTAIN?

- → Nicotine
- → Natural fibers
- → Flavourings
- → Sweeteners
- → Water

WHAT IS THE DIFFERENCE BETWEEN TRADITIONAL SNUS AND NIC-S?

- → NIC-S® is 100% tobacco-free, and we mean it. Our Pouches are made from completely non-tobacco derived nicotine
- → "All White" ingredients - does not stain the teeth
- → No tobacco smell or taste
- → Less salivation, no need to spit

CLOSING THE REGULATORY GAP FOR SYNTHETIC NICOTINE PRODUCTS

PATRICIA J. ZETTLER*
NATALIE HEMMERICH**
MICAH L. BERMAN***

Abstract: In July 2017 the U.S. Food and Drug Administration announced a new "comprehensive plan for tobacco and nicotine regulation." This plan focuses on making cigarettes less addictive while facilitating the development of alternative, and less-harmful, nicotine-containing products. This approach holds promise, and the public health stakes could not be higher—smoking is the leading cause of preventable death in the United States, resulting in roughly 480,000 deaths per year. But a new consumer product is emerging that could upset the FDA's plans for a well-balanced regulatory scheme: synthetic nicotine. Synthetic nicotine products currently fall into a regulatory gap because they do not appear to meet the Federal Food, Drug, and Cosmetic Act's definition of a tobacco product. If this gap remains in place, it is likely that more companies will choose to market synthetic nicotine products in order to evade regulation, undoing the potential benefits of the FDA's plan for tobacco and nicotine regulation. This Article argues that the FDA can, and should, address this problem by regulating synthetic nicotine products as drugs. After reviewing the science of nicotine addiction and the FDA's past and present regulatory schemes for nicotine, this Article explains how the FDA could establish that synthetic nicotine products are drugs under the FDCA's definition. This Article then concludes with a discussion of the policy benefits of categorizing synthetic nicotine products as drugs.

Boston College Law Review, 2018

FDA Official Says Tobacco Product Reviews Are in 'Final Stages'

Tiffany Kary

Published On 10:09 PM IST, 27 Oct 2021
Last Updated On 10:38 PM IST, 27 Oct 2021

(Bloomberg) -- The U.S. Food and Drug Administration is close to wrapping up a sweeping review of tobacco products sold in the U.S., though it faces a round of lawsuits challenging actions it has taken.

"Many of the reviews are in final stages," said Mitch Zeller, director of the agency's Center for Tobacco Products, speaking at a virtual conference hosted by the **Food and Drug Law Institute** Wednesday. Zeller said the agency has already refused to allow 200,000 products to continue being sold, has authorized only three, and has around 80,000 products pending. The FDA is being sued for 46 of the refusals.

Zeller said that some companies seek to circumvent FDA authority by using synthetic nicotine. This complicates the agency's efforts because the FDA has authority to regulate tobacco products, but regulations are hazier when it comes to synthetic nicotine. It's getting harder to tell the lab-made nicotine from the plant-derived version of it, and the agency is investigating the issue, Zeller said, adding that the FDA is talking to Congress about a potential legislative fix.

Bloomberg/Quint, 10/27/21

PIPER | SANDLER

Tobacco

Synthetic Nicotine Bursts on to the Scene

CONCLUSION

We recently visited the Tobacco Plus Expo (TPE) in Las Vegas, with 350+ exhibitors and 5,000+ attendees. Many new brands of nicotine pouches and vapor products used the show to help launch new products, all of which use synthetic nicotine (i.e. not derived from tobacco), and therefore are not subject to FDA regulations (like a PMTA review to be authorized for legal sale). While many of the vapor companies at the January 2020 show no longer had a presence (following a PMTA filing deadline in September 2020), tobacco-free nicotine (TFN) products were very prominent. TFN may be a golden ticket: no FDA regulation, no tobacco taxes, no flavor restrictions, and no restrictions on direct to consumer e-commerce. Near-term, these launches appear to increase competition for Altria, BAT and Imperial in nicotine pouches and vapor, but their existence suggests TFN is commercially viable, and therefore likely an opportunity for big players.

Piper/Sandler, 5/16/21

Federal Regulatory Options/Issues

- **FDA** could regulate synthetic nicotine under its authority to regulate “drug-delivery devices”
- **Congress** could redefine FDA’s tobacco-related regulatory authority to include recreational nicotine products regardless of source
  - If regulated differently, **testing** becomes an important issue

State/Local Responses

- Implications for scope of all tobacco-related law: licensing, taxes, flavor restrictions, smoke-free laws, Tobacco 21 laws, etc.

- **Chicago** just amended definition of "tobacco products" in its code:
  - "products containing nicotine derived from tobacco **or any other source"**

- **Wyoming**: "'Electronic cigarette' means any device that can be used to deliver aerosolized or vaporized nicotine or **synthetic nicotine**"

Final Notes

- “Tobacco-free” claims
- Confusion over amount of nicotine reported for racemic mixture
- Need or research on use, marketing, consumer perceptions, health effects

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