

Marketing of “Tobacco-Free” and “Synthetic Nicotine” Products

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White Paper

Stanford Research into the Impact of Tobacco Advertising

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RKJ conceptualized the study and was primary author of the paper.

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ABSTRACT

Aims: To characterize the scope and scale of “tobacco-free” and “synthetic nicotine” products on the market and their regulatory implications.

Design: Survey of nicotine products offered for sale online which claim either to be made from “synthetic nicotine” or that they are “tobacco-free.” Analyze the extent to which these novel products circumvent governmental regulations, tobacco taxation, and tobacco sales bans of major online marketplaces.

Findings: As the deadline for FDA authorization of novel tobacco products approached, a rapidly increasing number of brands assert that their products are not derived from tobacco and thus are exempt from the Agency’s regulations. Six manufacturers offer synthetic nicotine while others that claim to be “tobacco-free” use a purified form of tobacco derived nicotine. “Tobacco-free” labeling conveys advantages to the seller beyond exemption from tobacco regulation and taxation. Major online marketplaces, which prohibit both sales and paid advertising of tobacco products, allow them for brands claiming to be “tobacco-free.”

Conclusions: There is no rationale for products using non-tobacco sourced nicotine to be exempt from regulation. As nicotine is highly addictive, this regulatory loophole needs to be closed by designation as either a drug or tobacco product. These brands assert that they are not tobacco products, and many make reduced harm and even therapeutic claims. Logically, they are unauthorized drugs and should be removed from the market pending new product application. Those products claiming to be “tobacco-free,” which use highly purified tobacco-derived nicotine, are subject to existing FDA tobacco regulations.

Glossary of Terms

Synthetic Nicotine (SYN): Nicotine produced via synthesis using chemical precursors derived from non-tobacco sources.

Tobacco-Free Nicotine (TFN): A term loosely used by a number of emerging nicotine products, sometimes with ambiguous meaning. Technically, it should be a broad term encompassing synthetic nicotine and nicotine derived from other nightshade family plant sources such as tomato and eggplant. Some companies may be using this label inaccurately, describing their brands as “tobacco-free” but actually using a highly purified form of tobacco-derived nicotine or merely inaccurately labelling standard tobacco-derived nicotine. While “TFN” is the registered trademark of synthetic nicotine manufacturer Next Generation Labs, it is also used generically by many brands.

Tobacco Leaf-Free Nicotine: Term used by a handful of brands referring to a more highly purified form of tobacco-derived nicotine depleted of residual tobacco chemicals.

Nicotine Analogs: Any of a family of compounds which mimic the structure of nicotine. Some of these possess psychoactive and addictive properties.

Executive Summary:

- A 2009 US law assigned tobacco regulation to the FDA, created its Center for Tobacco Products, and defined a tobacco product as derived from any component of the tobacco plant.
- As the September 2020 deadline for submission of application to the for FDA authorization of novel tobacco products (PMTA) approached, major tobacco companies submitted application for their brands, but innumerable smaller companies lacked the resources needed to undertake the extensive studies required.
- In an effort to circumvent FDA tobacco regulations, and thus exempt their products from the PMTA process, numerous brands claimed to be formulated with tobacco-free and/or synthetic nicotine.
- Following the late 2021 denial of their PMTA applications, some brands which were ordered off the market promptly relaunched claiming that they had been reformulated with tobacco-free or synthetic nicotine.
- Brands claiming to use non-tobacco derived nicotine are offered in a wide array of youth-appealing sweet & fruity flavors – which have been systematically denied market authorization during the ongoing FDA PMTA process.
- Synthetic nicotine is currently expensive, costing approximately 4x tobacco derived nicotine.
- While residuals from tobacco leaf derived nicotine are well known, byproducts of the chemical synthesis of nicotine have not been characterized for potential human toxicity and carcinogenicity.
- Justified by concerns for unknown safety risk, the FDA should insist upon toxicity/carcinogenicity studies of synthetic nicotine products before they are marketed.
- The FDA should also consider systematic testing of products claiming to be tobacco-free as at least a portion of them may prove to have chemical signatures indicative of tobacco origin.
- Some brands marketed as “tobacco-free” or “tobacco leaf-free” use a purified form of tobacco derived nicotine and thus are legally tobacco products under US law and thus subject to the PMTA requirements.
- Terms describing nicotine products as “tobacco-free,” “non-tobacco,” and “zero tobacco” need regulation as consumers may perceive such products as having reduced addictive potential.
- Marketing claims such as “clean,” “pure,” and “free of carcinogens” should be disallowed absent modified risk designation by the FDA.
- “Tobacco-free” nicotine brands have been allowed to post paid advertisements, and are widely sold on major online stores (e.g., Amazon, eBay, Google Shopping), which prohibit sale of all tobacco products.
- Underage sales of “tobacco-free” nicotine products are common via major online stores.
- As it is a potently addictive substance, and harmful to the developing adolescent brain, there is no justification for nicotine, regardless of its source, to be exempt from regulation.
- The synthetic nicotine regulatory loophole should be closed by designating such products as unauthorized drugs requiring pre-market authorization.

INTRODUCTION

In 2009, the US Congress passed the Family Smoking Prevention and Tobacco Control Act which empowered the Food and Drug Administration (FDA) to regulate tobacco products and created its Center for Tobacco Products.¹ This law, which primarily focused on combustible cigarettes, defined a covered tobacco product as *“any product made or derived from tobacco that is intended for human consumption including any component, part, or accessory of a tobacco product.”* This definition includes any and all parts of the tobacco plant and has been interpreted to include tobacco derived nicotine (TDN).

2009 US Law

Definition of a “Tobacco Product”

“Any product made or derived from tobacco that is intended for human consumption including any component, part, or accessory of a tobacco product.”

Public Law 111–31
111th Congress

An Act


To protect the public health by providing the Food and Drug Administration with certain authority to regulate tobacco products, to amend title 5, United States Code, to make certain modifications in the Thrift Savings Plan, the Civil Service Retirement System, and the Federal Employees’ Retirement System, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

DIVISION A—FAMILY SMOKING PREVENTION AND TOBACCO CONTROL ACT

June 22, 2009
[H.R. 1256]

Family Smoking Prevention and Tobacco Control Act.



Tobacco Plant

The original scope of the 2009 law did not encompass newly emerging tobacco products until, following a lengthy bureaucratic process, additional categories such as e-cigarettes were “deemed” to be within FDA purview in 2016.² After several more years delay, the FDA required submission of Premarket Tobacco Application (PMTA) for new tobacco products with authorization decisions by September 2021.³

¹ Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, 123 Stat. 1776. 2009.
<https://www.congress.gov/bill/111thcongress/house-bill/1256..>

² US Food and Drug Administration. Deeming Regulations for E-Cigarettes, Cigars, and All Other Tobacco Products as Amended by the Family Smoking Prevention and Tobacco Control Act.
<http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm394909.htm>.

³ US Food and Drug Administration. Premarket Tobacco Product Application. <https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/premarket-tobacco-product-applications>.

<p>Public Law 111-31 111th Congress</p> <p>An Act</p> <p>To protect the public health by providing the Food and Drug Administration with certain authority to regulate tobacco products, to amend title 5, United States Code, to make certain modifications in the Thrift Savings Plan, the Civil Service Retirement System, and the Federal Employees' Retirement System, and for other purposes.</p> <p>Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,</p> <p>DIVISION A—FAMILY SMOKING PREVENTION AND TOBACCO CONTROL ACT</p> <p>Family Smoking Prevention and Tobacco Control Act.</p>	<p>2009 FDA CTP Created</p>	
	<p>2016 Emerging Products (e.g. e-Cigarettes) "Deemed"</p>	
	<p>2019 PMTA Process Due Sept 2020 Decision Sept 2021</p>	

While the FDA estimates the cost of preparing a PMTA on the order of a few hundred thousand dollars, industry insiders put the estimate in the tens of millions of dollars, due to the requirements for detailed scientific and technical data as well as for separate applications for each different variation of the brand (e.g., flavors, nicotine concentrations).^{4 5} While well within the financial capability of major tobacco companies, such an outlay lies beyond the fiscal resources of a large swath of smaller e-cigarette companies. As the deadline for the PMTA approached, a surge of nicotine containing brands emerged on the US market sporting claims such as “tobacco-free nicotine” (TFN) and/or “synthetic nicotine” (SYN) with the goal of being exempted from FDA regulation.^{6 7 8 9 10} These include a number of products such as e-cigarettes, e-liquids, and

⁴ US Food and Drug Administration. Questions on FDA's New Regulations for E-Cigarettes, Cigars, and All Other Tobacco Products: What are the costs associated with submitting an application? <https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/commonly-asked-questions-about-center-tobacco-products#1>.

⁵ Duprey R. Big Tobacco Is About to Dominate the E-Cig Industry. The Motley Fool. September 3, 2020. <https://www.fool.com/investing/2020/09/03/big-tobacco-is-about-to-dominate-the-e-cig-industry/>.

⁶ Ducharme J. Some vaping companies are turning to synthetic nicotine to outsmart the FDA. Time Magazine. September 17, 2021. Available at <https://time.com/6098897/vaping-companies-synthetic-nicotine/>.

⁷ Westcoast Vape Supply. Will 2021 be the year for synthetic nicotine? <https://westcoastvapesupply.com/blogs/updates/will-2021-be-the-year-for-synthetic-nicotine>.

⁸ Cwalina SN, McConnell R, Benowitz NL, Barrington-Trimis JL. Tobacco-free Nicotine - New Name, Same Scheme? N Engl J Med. 2021 Dec 23;385(26):2406-2408.

⁹ Jordt SE. Synthetic nicotine has arrived. Tob Control. 2021 Sep 7. doi: 10.1136/tobaccocontrol-2021-056626. PMID: 34493630.

¹⁰ Foley KE. Synthetic nicotine: Unregulated and increasingly popular. Politico. February 7, 2022 <https://www.politico.com/news/2022/02/07/unregulated-synthetic-vape-growing-kids-00005932>

recreational oral nicotine products (e.g., pouches, gums, lozenges, toothpicks). The tactical value of TFN/SYN to companies that lack the resources to complete a PMTA application was well articulated by an e-liquid company: “Now that the FDA's PMTA deadline has passed, vapor businesses which could not afford to submit an application are looking for any loophole in the regulations that could allow them to stay in business.”¹¹

The goal of this study is to characterize the scope and scale of TFN/SYN products on the market and their promotional claims. We will also examine the ways these brands seek to circumvent governmental regulatory requirements, be exempted from tobacco taxation, and bypass tobacco sales prohibitions of online marketplaces.

Faced with a steady decline in cigarette sales, major tobacco companies are diversifying the product lines to include a variety of nicotine delivery systems such as e-cigarettes, heated tobacco, and oral pouches. While major tobacco companies can afford the high cost of PMTA submissions, often costing tens of millions of dollars, thousands of small brands cannot afford this investment. Many have converted their products to “non-tobacco” sourced nicotine as a means of circumventing the PMTA process.



¹¹ The Synthetic Nicotine Loophole. Kai's Virgin Vapor Blog. October 27, 2020.
<https://www.kaisvirginvapor.com/blogs/news/the-synthetic-nicotine-loophole>.

METHODS

Identification of SYN manufacturers and retail TFN/SYN brands involved keyword searches on Google, patents and trademark databases, and online vendors of tobacco products. **(See Supplement)** The websites of the top 15 online vendors most frequently listed from our Google keyword searches were then examined for SYN and TFN products. To identify the most prominent vendors, rankings across 9 search terms were aggregated and scored. TFN and SYN brand promotional activities were collected from company websites, branded social media posts (Instagram, Facebook), press releases, earned media, and media interviews by company leaders. Samples of SYN and TFN products were purchased through US online vendors. Packaging nicotine addiction warning labels were examined and inconsistencies with FDA labeling requirements for tobacco products were noted.

Price comparison of SYN versus TDN was conducted via both wholesale and retail sellers. Major online marketplace sellers (Amazon, e-Bay, Google Shopping, Target, and Walmart) were searched for listings of TFN and SYN products for sale. Major tobacco company TFN and SYN brands were searched for individually (ZYN, ON!, Rogue, Velo, etc.) as were generic terms such as “oral nicotine pouches.” Instances of paid advertising of TFN and SYN brands on online marketplaces were noted.

Major online vendors such as Amazon, e-Bay, Google Shopping, Target, and Walmart were searched for listings of TFN/SYN products for sale. Leading TFN/SYN brands were searched for individually (ZYN, 2One, ON!, Rogue, Velo, etc.) as were generic terms such as “oral nicotine pouches.” Instances of paid advertising of TFN/SYN brands on online store websites were noted.

To check whether underage sales of TFN/SYN products were possible via Amazon and e-Bay, we created a Gmail identity of a 14-year-old boy and then created accounts using his identity with both online stores. The “synthetic” teenager then purchased of TFN/SYN products using either a company gift card of the type widely available online and in retail settings such as supermarkets, convenience stores, and chain pharmacies or a VISA debit gift card.

BACKGROUND:


Development of Synthetic Nicotine

After centuries of selective cultivation, commercial tobacco plants are highly efficient in producing abundant nicotine which can be extracted economically and marketed as a bulk chemical product. Nicotine is also produced by a variety of plants in the nightshade family such as tomato, potato, and eggplant to ward off insect predators. The minute quantities of nicotine make these plant sources commercially impractical.¹² Recently, the regulatory genes responsible for nicotine synthesis in tobacco (e.g. nicotine synthetase) have been elaborated and genetic


¹² Domino EF, Hornbach E, Demana T. The nicotine content of common vegetables. *N Engl J Med.* 1993; 329:437.


methods to boost nicotine production patented.^{13 14} It is theoretically possible, via genetic manipulation, to achieve commercially viable nicotine production in quantity, for example, in tomato or eggplant.¹⁵

Non-Tobacco Nicotine Sources: Nightshade Plants & Synthetic Nicotine




Tobacco Plant






Nightshade Plants



Synthetic Nicotine Patent



NextGenerationLabs

**United States
Patent Application Publication
Balder**

SYNTHETIC OR IMITATION NICOTINE
COMPOSITIONS, PROCESSES AND
METHODS OF MANUFACTURE (52)

**Pub. No.: US 2014/0261507 A1
Pub. Date: Sep. 18, 2014**

Nicotine was first synthesized by Swiss chemist Amé Pictet in 1904.¹⁶ Because extracting nicotine from tobacco leaf is efficient and inexpensive, while synthesis from precursor compounds relatively complex and expensive, for over a century synthetic nicotine had no commercial role. A series of patents have appeared in recent years describing various methods of synthesizing nicotine from non-tobacco precursor products. NextGenerationLab’s (NGL) patent for its TFN® product, which is noteworthy due to its market leadership, uses nicotine acid esters as a precursor.¹⁷

Synthetic Nicotine Chirality

Some molecules, such as nicotine, may exist in mirror image forms with identical chemical make up but sometimes differing biological activity. The nicotine molecule possesses chirality,

¹³ Wang, B., Lewis, R., Shi, J. et al. Genetic Factors for Enhancement of Nicotine Levels in Cultivated Tobacco. *Sci Rep.* 2015;5:1-10.

¹⁴ Redington, T. European Patent Allowed for 22nd Century’s Nicotine Biosynthesis Genes. Published Nov 29, 2013. Available at <http://www.businesswire.com/news/home/20131129005312/en#.U8BLtmx3seg>. Accessed July 23, 2021.

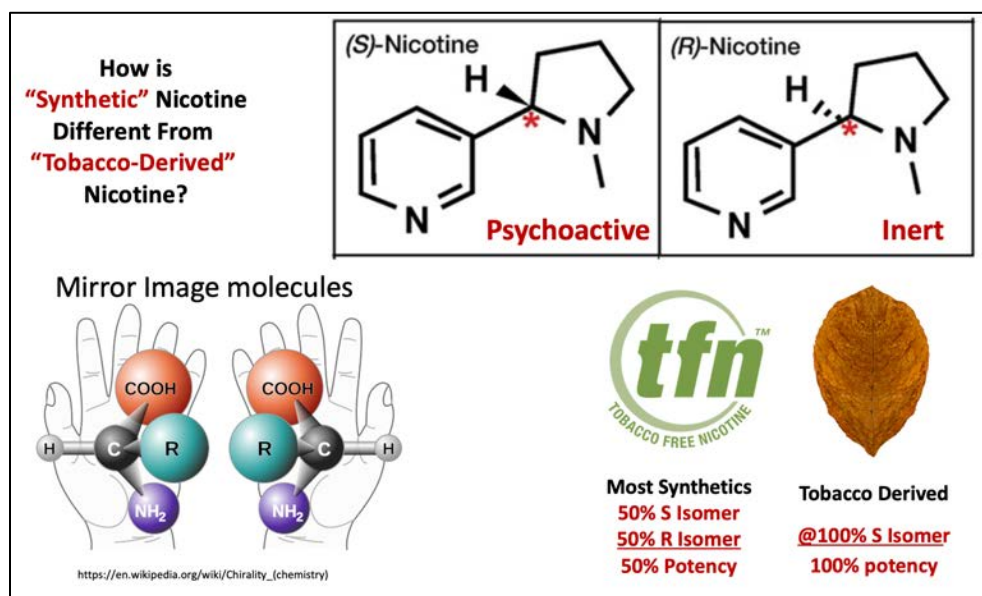
¹⁵ Hayashi S, Watanabe M, Kobayashi M, Tohge T, Hashimoto T, Shoji T. Genetic Manipulation of Transcriptional Regulators Alters Nicotine Biosynthesis in Tobacco. *Plant Cell Physiol.* 2020;61:1041-53.

¹⁶ Pictet A, Rotschy A. Synthese des Nicotins. *Berichte Dtsch Chem Ges.* 1904;37:1225–35.

¹⁷ Kaufman JG. Nicotinic acid esters. *J. Am. Chem. Soc.* 1945; 67:497–498.

meaning it exists in two mirror image versions called enantiomers or stereoisomers. Nicotine comes in a left (S) and right (R) forms. The S isomer of nicotine greatly predominates in tobacco leaf which contain only small amounts of the R variant (0.1 to 1.2%).¹⁸

Studies in animals indicate that the R stereoisomer is substantially less potent physiologically than the S.¹⁹ Synthetic nicotine, such as NGL’s TFN®, are racemic meaning that they thus contain an equal blend of the S and R stereoisomers.²⁰ This implies that racemic synthetic nicotine in similar concentration of TDN will have roughly one half the potency in terms of satisfying addictive urges. Kaival Labs, which purchased the synthetic nicotine patents of NextGenerationLabs in October 2020, claims in a public relations release under the title “Effective and Satisfying, Yet Addiction Free” that adjustment of the R vs. S ratio may produce “non-addictive nicotine” that could serve as a “true step down product.”²¹ ²²Given the lack of human studies of the addictive impact of differing nicotine stereoisomer combinations, this assertion is notably speculative. Recently, selective synthesis of the active S-isomer has been described.²³



¹⁸ Armstrong DW, Wang X, Ercal N. Enantiomeric composition of nicotine in smokeless tobacco, medicinal products, and commercial reagents. *Chirality*. 1998;10:587-91.

¹⁹ Risner ME, Cone EJ, Benowitz NL, Jacob PI. Effects of the stereoisomers of nicotine and nornicotine on schedule-controlled responding and physiological parameters of dogs. *JPET*. 1988;244:807-13.

²⁰ Hellinghausen G, Lee JT, Weatherly CA, Lopez DA, Armstrong DW. Evaluation of nicotine in tobacco-free commercial products. *Drug Test. Anal.* 2017;9: 944-48.

²¹ NextGenerationLabs patent assigned to Kaival Labs Inc. Published October 19, 2020. Available at <https://patents.google.com/patent/US20170189388A1/en>. Accessed July 23, 2021.

²² Desperate Need Fuels New Products, Programs in Smoking Cessation Space. PR Wire. Published September 29, 2020. <https://www.prnewswire.com/news-releases/desperate-need-fuels-new-products-programs-in-smoking-cessation-space-301139492.html>

²³ Panda B, Albano G. Synthetic Methods for the Preparation of Conformationally Restricted Analogues of Nicotine. *Molecules*. 2021 Dec 13;26(24):7544.

RESULTS

Synthetic Nicotine Manufacturers

We were able to identify 6 companies which claim to manufacture synthetic nicotine.^{24,25,26,27,28,29,30} SYNs are marketed as appropriate for use in a wide array of non-combustible nicotine products, both recreational and therapeutic (i.e. smoking cessation products). The market leader Next Generation Labs (NGL) (founded 2014) claims that its TFN[®] product is formulated in at least 60 retail nicotine products.³¹ While SYN manufacturers typically sell bulk nicotine to companies who integrate it into retail products, we identified instances in which the manufacturers also produced consumer products. In 2017, NGL announced it was planning to offer a nicotine product under the brand name “Zia Gum” which we could not identify on the market in 2021.³² NGL and the TFN[®] retail oral pouch brand 2One have the same CEO.³³

Synthetic Nicotine Brands:

TFN is a product of Next Generation Labs (<https://www.nextgenerationlabs.com>). SyNic is marketed by Zanolprima Lifesciences (<https://www.zanolprima.com>). Syntha is made by Nude Nicotine (<https://nudenicotine.com>). Chemnovatic, Hangsen, and CNT are company names.



²⁴ NextGenerationLabs. Tobacco Free Nicotine. <https://www.nextgenerationlabs.com>.

²⁵ Zanolprima. Trademark application for SyNic. <https://alter.com/trademarks/synic-79296455>

²⁶ Hangsen Tech. Synthetic Nicotine. <http://www.hkhangsen.com/show/index/cid/7/id/6.html>

²⁷ CHEMNOVATIC. Synthetic Nicotine. Available at <https://chemnovatic.com/product/synthetic-nicotine-995-usp-ep/>

²⁸ Schmid T. A real up and comer: Synthetic nicotine. February 14, 2021. <https://www.tobaccoasia.com/features/a-realup-and-comer-synthetic-nicotine/>

²⁹ Nude Nicotine. Syntha. <https://nudenicotine.com/collections/syntha>

³⁰ Five Pawns. S-isomer tobacco free nicotine. Five Pawns. January 4, 2021. <https://fivepawns.com/blogs/five-pawns-news-events/s-isomer-tobacco-free-nicotine>

³¹ Next Generation Labs warns of surge in fake and counterfeit synthetic nicotine products coming from China. PR Wire. September 17, 2020. https://www.prweb.com/releases/next_generation_labs_warns_of_surge_in_fake_and_counterfeit_synthetic_nicotine_vape_products_coming_from_china/prweb17398859.htm

³² Next Generation Labs CEO Vincent Schuman announces ZIA Gum with TFN Synthetic nicotine. October 31, 2017. <https://www.streetinsider.com/Press+Releases/Next+Generation+Labs+CEO+Vincent+Schuman+Announces+ZIA%E2%84%A2+Gum+with+TFN%C2%AE+Synthetic+Nicotine/13442562.html>

³³ Prokov H. 2One Labs Launches Nontobacco-Derived Nicotine Pouch. CSP. November 19, 2020. <https://www.cspdailynews.com/tobacco/2one-labs-launches-nontobacco-derived-nicotine-pouch>.

Highly Purified Tobacco Derived Nicotine Marketed as “Tobacco-Free”

Contraf-Nicotex-Tobacco (CNT) (Germany) is a major supplier of highly purified pharmaceutical TDN, which it markets as “nicotine in its purest form” and having “ultralow impurity levels.”³⁴ It is suspected that some brands have labeled such highly purified TDN as “non-tobacco” or “tobacco free.”

Price Comparison of Tobacco Derived Versus Synthetic Nicotine

A December 2021 price comparison of products listed on Liquid Nicotine Wholesalers showed the wholesale price of synthetic NGL TFN® (1 gallon of 100mg/ml or 10%) in vegetable glycerin was \$750 per gallon whereas similar TDN ranged from \$165 to \$220.³⁵ SYN manufacturer Syntha offers 1 liter of 100 mg/ml SYN in its racemic form (equal mixture of R+S stereoisomers) for \$1,240/L versus \$1,970/L for its stereoselective S isomer product.

Most nicotine brands (e.g., e-cigarettes, e-liquids, pouches, gums, lozenges), whether TDN or nicotine versions are offered at identical prices, an indication that the cost of the higher priced SYN nicotine is not being passed on to the consumer.

Price comparison (February 2022) of synthetic vs. tobacco-source nicotine.


LIQUID NICOTINE WHOLESALE

Synthetic vs. Tobacco-Sourced Nicotine Salts (250mg/ml)

Synthetic Nicotine \$1929.99/Gallon


TFN® 250mg Nicotine Salt
Tobacco Free Nicotine Salt
100% PG Dilution Available in 5+ Gallon Sizes
TFN Nicotine is In Stock.
★★★★★ 1 Review

\$1929.99

Buy 4 for \$1684.99 each and save 13%

* Nicotine Content (mg/mL)
250mg

* Bottle Size
1 Gallon 5 Gallons

* Base
100VG

1 **ADD TO CART**

Tobacco-Derived Nicotine \$469.99/Gallon


250mg Nicotine Salts

Salt Nicotine Solution
100% PG Dilution Available in 5+ Gallon Sizes
★★★★★ 22 Reviews

\$469.99

* Nicotine Content (mg/mL)
250mg

* Bottle Size
1 Gallon 5 Gallons

* Base
100VG

1 **ADD TO CART**









Synthetic Nicotine Cost @ 4x > Tobacco-Derived

<https://liquidnicotinewholesalers.com/250mg-nicotine-salts.html>

³⁴ Contraf-Nicotex-Tobacco. About us. <https://cntgroup.de/our-business/>

³⁵ Liquid Nicotine Wholesalers. USP nicotine liquid. Available at <https://liquidnicotinewholesalers.com/bulk-usp-nicotine-liquid.html>

Comparison of “Tobacco-free” and “Tobacco leaf-free” prices of oral nicotine pouches offered by major tobacco companies with their conventional tobacco pouches. This suggest that tobacco companies are not passing through the higher cost of “non-tobacco” sourced nicotine products to consumers. Indeed, RJ Reynolds “Tobacco leaf-free” pouch Velo is notably less expensive than their tobacco snus.

Price Comparison Tobacco and “Non-Tobacco” Pouches of Major Tobacco Companies					Tobacco Pouches	“Non-Tobacco” Pouches
	Brand	#Pouches per Can	Price	Price/Pouch*		
Swedish Match.	General	24	\$6.19	\$0.26		
	Zyn	20	\$4.89	\$0.24		
	Camel Snus	15	\$5.09	\$0.34		
	Velo	20	\$4.29	\$0.21		
	Marlboro Snus	Discontinued	-	-		
	On!	20	\$4.29	\$0.21		


Prices from Northerner: <https://www.northerner.com/us>

“Tobacco leaf-free” on! brand (Altria) price remains constant at various nicotine concentrations. This is a sign that tobacco companies are not passing through the higher cost of “non-tobacco” nicotine in these products to consumers.


on!

Strength


1.5mg	2mg	3.5mg	4mg	8mg
\$4.39	\$4.39	\$4.39	\$4.39	\$4.39



1.5 MG BERRY
20 NICOTINE POUCHES
WARNING: This product contains nicotine. Nicotine is an addictive chemical.



2 MG BERRY
20 NICOTINE POUCHES
WARNING: This product contains nicotine. Nicotine is an addictive chemical.



3.5 MG BERRY
20 NICOTINE POUCHES
WARNING: This product contains nicotine. Nicotine is an addictive chemical.



4 MG BERRY
20 NICOTINE POUCHES
WARNING: This product contains nicotine. Nicotine is an addictive chemical.



8 MG BERRY
20 NICOTINE POUCHES
WARNING: This product contains nicotine. Nicotine is an addictive chemical.

Scope and Scale of “Tobacco-Free” and “Synthetic Nicotine” Marketplace

Marketers of purportedly non-tobacco nicotine products label their products in three ways: synthetic, tobacco-free, and tobacco leaf-free. We identified 98 brands claiming to contain “synthetic nicotine.” Some disposable e-cigarettes incorporate synthetic messaging in their brand name (e.g. SYN Bar, SYN Sticks). As a means of estimating the scope of the marketplace, the SYN and TFN offerings of 15 leading online vendors were analyzed. A wide variety of e-liquids, disposable e-cigarettes, and pouches were found.

Brands use term such as “synthetic,” “tobacco-free,” “zero tobacco,” non-tobacco,” and “tobacco leaf-free.” Swedish match’s Zyn has the highest sales among nicotine pouch brands in the US. Velo is a product of multinational tobacco company RJ Reynolds.



Examples of nicotine e-Liquids marketed as “synthetic nicotine” and/or “tobacco-free.”



Examples of disposable e-cigarettes marketed as “synthetic nicotine” and/or “tobacco-free.”



Examples of nicotine pouches marketed as “synthetic nicotine” and/or “tobacco-free.”



Tobacco products with variations of the term “synthetic” in their brand names.

Leading oral pouch brand ZYN is a synonym of SYN.







Table on Next Page:

Recreational nicotine products (150) marketed as having: “synthetic,” “tobacco-free,” or “tobacco leaf-free” nicotine as surveyed in February 2022. Marketing claims were derived from the brand’s website, its packaging, or retail promotion.

Marketing Claims	Oral Pouches (39)	Gums (4)	Disposable e-Cigarettes (44)	e-Liquids (63)
“Synthetic” Nicotine (98)	2one Fr3sh Fully Loaded niin Rococo Sattwa White Fox	Zia	Air Factory Beast Synthetic BlueBar BLVD 3K Captain Fog Doo Dinner Lady Exotic Bar Geek Bar H&S Synthetic Haven Helix Bar Helo Juice Head Glamee Nova Ignite Infuse infzn I love salts KangVape Monster Bar NIIN Next Bar Pachamama Puff Labs Pod Mesh 5500 Loaded Ruthless R&M Synthetic Real Stick Rev SYN Steam Engine Nunu SWFT SYN Bar SYN Sticks	Air Factory SYNNIC Aqua Alt Zero Bad Drip Bantam Camarosa Coastal Cloud Cloud Heads Cloud Nurdz Dinner Lady Enfuse Excision Frozen Fruit Feellife Freeman Fruit Monster Frisco Vapor Method Fryd Glas BSX Jam Monster Juice Head Juice Roll Upz Keep it 100 Killa Kilo Revival Liquid EFX Lost Art Liquids Loaded Mega Salt Juice Mighty Vapors
“Tobacco Free” Nicotine (44)	4nx 77 &Boost Ace Bidi Candy Fre Fixx G.3 Klint Killa Lucy Lyft Nic-S	NOIS Nordic Spirit Rush Salt BrewCo Swave Thunder Volt Vika Blue Whitetail Zafari ZoneX Zyn X-Range XQS	Breeze Pro Cali Bar 2k Chubby EPIC Flurry Lucid Air Mr. Fog Puff Bar VapeSoul Vegaz	Cloud Nurdz Custard Monster Glas Humble Juice Co. Moo Eliquids Salty Man Vapor
“Tobacco Leaf-Free” Nicotine (7)	Black Buffalo On! Rogue Velo	Lucy Rogue Solace		

Survey of product lines which carry the description of either “tobacco-free” or “synthetic” nicotine offered for sale by 15 leading online vendors of tobacco products identified via Google search (July 2021). List includes the number of brands as well as the number of products, the latter being greater due to brands being offered in multiple flavors and nicotine concentrations. These data are not cumulative as multiple vendors offer the same brands and products.

<div>     </div>				
Online Vendors	"Synthetic" Nicotine Brands	"Synthetic" Nicotine Products	"Tobacco-Free" Nicotine Brands	"Tobacco-Free" Nicotine Products
Electric Tobacconist	17	137	16	149
Element Vape	15	119	6	26
eJuices.com	11	147	6	57
Eight Vape	8	58	15	114
Direct Vapor	5	39	1	1
Vapor Beast	5	53	3	9
Vape Royalty	4	42	3	34
Flawless Vape Shop	3	32	2	8
Giant Vapes	3	19	9	38
VaporFi	2	17	0	0
Vapor Authority	2	28	1	3
Vaping.com	2	22	14	73
myvpro	1	4	4	28
VaporDNA	0	0	5	38
UK ecig store	0	0	1	5

Advertising Claims of SYN Manufacturers and SYN/TFN Consumer Brands

Many SYN products claim to be “99+% pure” and contain only “clean nicotine” and thus are “tasteless and odorless,” implying that TDN impairs undesirable “off flavor” sensory characteristics.²⁷ SYN manufacturer NGL uses the slogan “Putting the flavor back in vaping” for its TFN[®] product and claims to be “devoid of many of the residual impurities that tobacco derived nicotine (TDN) contain.”²⁷ Some brands have gone so far as to claim they have fewer carcinogens.³⁶ According to the company’s CEO, Zanoprima’s SyNic product is “a new synthetic nicotine coming to market has none of the possible cancer-causing impurities that are found in traditional leaf-derived nicotine.”³⁷ Some of the products’ promotional materials mention the potential regulatory advantages of using non-tobacco sourced nicotine. (**Table 1**)

³⁶ Schmid T. A real up and comer: synthetic nicotine. Tobacco Asia. Published February 14, 2021. Available at <https://www.tobaccoasia.com/features/a-real-up-and-comer-synthetic-nicotine/>

³⁷ Donohue T. A new version of synthetic nicotine eliminates the cancer-causing impurities in leaf-derived nicotine. Vaporvoice. Published October 12, 2020. Available at <https://vaporvoice.net/2020/10/12/disruptive-science/>.

There is a similar emphasis on the cleanliness and purity of nicotine. Niin TM (short for “nicotine innovated”) claims on their website that its SYN pouches lack the “numerous residual impurities” of TDN.³⁸ Nicotine pouch brand ZYN claims it is: “.. made with pharmaceutical-grade nicotine salt, along with other natural and artificial ingredients, for a cleaner nicotine experience.”³⁹ Lucy Gum, which uses TDN described as “tobacco leaf-free,” advertises with slogans such as: “Clean nicotine that tastes great,” “Always have some tasty clean nicotine when the mood strikes,” “We’ve got nothing to hide (unlike those other guys),” and “A tasty, buzzy, smoke-free option instead of a cigarette.”⁴⁰

Product descriptors used by 6 purveyors of synthetic nicotine. Note the marketing emphasis upon purity, cleanliness, taste/aroma when the real reason for brands to use these products is regulatory escape. Electronic cigarettes with high concentrations of tobacco-derived nicotine salts come in a wide variety of flavors, many of which are sweet or fruity, and have gained wide popularity among consumers. Hence, there is little rationale for using much more costly synthetic nicotine for reasons of its supposed sensory benefits.

						
Purity	✓	✓		✓	✓	✓
Cleanliness	✓		✓		✓	✓
Taste/Aroma	✓	✓	✓	✓		
Color		✓	✓	✓	✓	
“Premium”	✓	✓			✓	
Chirality*	R+S			S-only	S-only	R+S S-only
Regulation				✓	✓	

* The S-isomer of nicotine is the psychoactive form. Tobacco-derived nicotine is nearly pure S-isomer while most synthetic nicotine is racemic (a mixture of R + S isomers)

³⁸ NIIN. The evolution of nicotine. Available at <https://niinpouches.com/>.

³⁹ Zyn. Why Zyn. Available at <https://us.zyn.com/why-zyn/>

⁴⁰ Lucy Gum. The future of nicotine. Available at <https://lucy.co/>

SRITA Collection of Non-Tobacco Sourced Nicotine Images**Synthetic Nicotine:**

https://tobacco.stanford.edu/pouches_gums/syntheticnicotine/synnic/

“Tobacco-Free” Nicotine:

https://tobacco.stanford.edu/pouches_gums/syntheticnicotine/tobaccofree/

“Tobacco Leaf-Free” Nicotine:

https://tobacco.stanford.edu/pouches_gums/syntheticnicotine/leaffreenic/



382 images as of February 5, 2022 (continuously updated)
https://tobacco.stanford.edu/pouches_gums/syntheticnicotine/

Examples of SYN/TFN product advertising from the SRITA Collection

FIND YOUR PROFITS. FIND YOUR FUTURE. FIND YOUR ZYN

ZYN TOBACCO-FREE NICOTINE POUCHES

WARNING: This product contains nicotine. Nicotine is an addictive chemical.

ZYN TOBACCO-FREE NICOTINE POUCHES

BUY 2 CANS SAVE \$1.00 OR BUY 1 ROLL SAVE \$3.00

THIS OFFER SAVINGS IS NOT AVAILABLE IN ALL AREAS.

WARNING: This product contains nicotine. Nicotine is an addictive chemical.

ZYN TOBACCO-FREE NICOTINE POUCHES

NOW AVAILABLE NATIONWIDE
CONTACT YOUR SWEDESH MATCH REPRESENTATIVE OR
CALL 800-367-3677 FOR ADDITIONAL DETAILS

EXPERIENCE ZYN

ZYN ONLY \$1.99

SYNTHETICS EJUICE

STRAWBERRY COTTON CANDY

SYNTHETICS EJUICE

STRAWBERRY COTTON CANDY

TASTE TEST

ZOOKA SYNTHETIC: GREEN APPLE

Tobacco Free Nicotine

8 Vapes

WARNING: This product contains nicotine. Nicotine is an addictive chemical.

NIC-S

FIVE FLAVORS. THREE STRENGTHS.

NIC-S* 100% TOBACCO-FREE NICOTINE POUCHES

PREMIUM FLAVORS MADE FROM THE HIGHEST-QUALITY INGREDIENTS

NIIN ZERO TOBACCO - PRIMED POUCHES™

ZERO TOBACCO™ NICOTINE POUCHES - CINNAMON
\$3.99 - \$18.99

ZERO TOBACCO™ NICOTINE POUCHES - CITRUS CHILL
\$3.99 - \$18.99

ZERO TOBACCO™ NICOTINE POUCHES - COOL MINT
\$3.99 - \$18.99

ZERO TOBACCO™ NICOTINE POUCHES - WINTERGREEN
\$3.99 - \$18.99

ZERO TOBACCO™ NICOTINE POUCHES - SPEARMINT
\$3.99 - \$18.99

Puff Labs BEAST SYNTHETIC Disposable | 2000+ Puffs - Lush ICE

\$24.95

ADD TO CART

Puff Labs BEAST SYNTHETIC Disposable Lush ICE

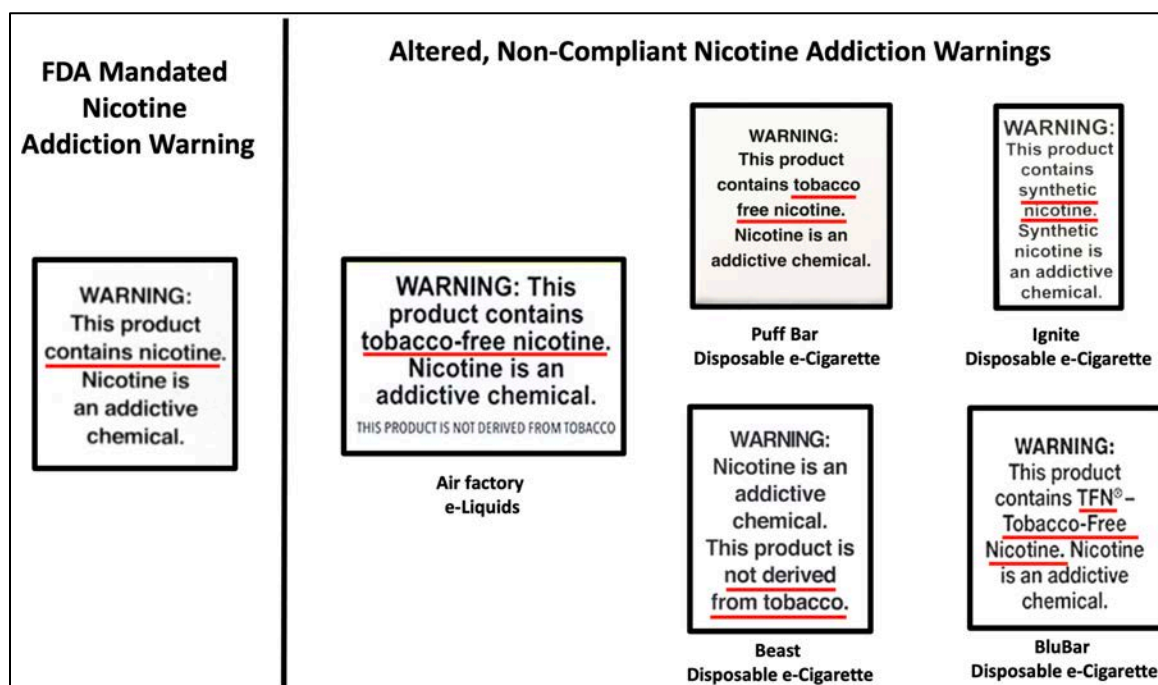
Flavor Profile: A fruity mixture of crisp watermelon and icy cold menthol.

The Puff Labs BEAST SYNTHETIC Disposable is a rechargeable sub ohm style disposable. Featuring a sub ohm style coil head for maximum flavor while being paired with 5% synthetic nicotine. This all new proprietary coil design allows for the purest and strongest flavor production out of any other disposable currently on the market. The BEAST SYNTHETIC is a compact, lightweight, and portable system that allows users to puff away without having to worry about anything. If your battery dies before the E-Liquid is gone, simply plug it in and re-charge it. Pre-filled with 6.0mL of Synthetic Nicotine and available in multiple flavor profiles, this is the perfect on-the-go device. Each Puff Labs Synthetic Disposable has an integrated and re-chargeable 1000mAh battery and lasts for 2000+ puffs.

Addiction Warning Labels

The FDA has issued highly specific requirements for both the wording and formatting of nicotine addiction warnings in tobacco products. If synthetic nicotine lies outside of FDA authority, then technically these labeling requirements would not apply. Many purportedly “non-tobacco” nicotine containing brands alter the mandated language.

Products that claim to use synthetic and/or tobacco-free nicotine alter the FDA’s legally mandated addiction warning labeling text. If synthetic nicotine lies outside of FDA authority, then technically these labeling requirements would not apply. To consumers, messages such as “tobacco-free” and “synthetic nicotine” may be perceived to connote reduced risk of addiction.



Ambiguities in “Tobacco-Free” and “Synthetic Nicotine” Brand Labelling

Technically, “tobacco-free” means that no part of the product comes derives from the tobacco plant (leaves, stems, roots, or seeds). It is suspected that some companies mislabel tobacco derived products as “tobacco-free,” “zero tobacco,” “non-tobacco,” or “tobacco-leaf free.” It is not only small independents which use such marketing terms for TDN. Leading recreational nicotine pouch brand Swedish Match (ZYN) describe its nicotine pouches as “tobacco-free” despite the fact that they use TDN.⁴¹ Other majors including Altria (ON!), RJ Reynolds (Velo), and Swisher Sweets (Rogue) term their oral recreational nicotine products “tobacco leaf-free” as does startup brand Lucy Gum. We also identified numerous brands claiming to use SYN, only a fraction of which specify the manufacturer (eg. TFN®, SYN®). The NGL trademarked brand name TFN® is often used as a generic marketing term (i.e. TFN).

⁴¹ Zyn. How are nicotine pouches made? Available at <https://uk.zyn.com/blog/behind-zyn/how-nicotine-pouches-are-made/>.

Exemption from Tobacco Taxation:

Some companies employing SYN may appear to be claiming exemption from tobacco taxation.⁴² For example: “Since NIIN™ Primed Pouches are a non-tobacco product, they are not subject to any tobacco-related excise taxes.”⁴³ A Chinese disposable SYN e-cigarette promotes itself as avoiding tax problems.⁴⁴ South Korea’s Custom Agency expressed concern over “skyrocketing” importation of tax-exempt forms of nicotine.⁴⁵

“Synthetic Nicotine” disposable e-cigarette brand R&M claims that it offers:

“No Tax Issue” and “No PMTA Issue.”



Sales of “Tobacco-Free” Brands via Online Stores

We identified 6 major online marketplaces that sell TFN and SYN products: Google shopping (15 brands), Target (12), Kmart (9), eBay (4), Amazon (3), and Walmart (1). None of these vendors offer cigarettes, cigars, or other long established tobacco products online. It may

⁴² Chaloupka FJ, Tauras JA. Taxation of emerging tobacco products. Tobacconomics. Published February 2020. Available at <https://tobacconomics.org/uploads/misc/2020/02/Emer.-Tob.-Tax.-Report-Relayout.pdf>

⁴³ Synthetic Nicotine Brand NIIN™ Launches with its Flagship 100% Tobacco-Free Synthetic Nicotine Pouches Line. February 11, 2021. http://finance.azcentral.com/azcentral/news/read/40980290/synthetic_nicotine_brand_niin%E2%84%A2_launches_with_its_flagship_100_tobacco.

⁴⁴ R&M Ultimate. Why choose a synthetic nicotine vape pen. Published January 22, 2022. Available at <https://www.rmultimate.com/Why-choose-Synthetic-nicotine-disposable-vape-pen-by-Bess-id3472101.html>




















⁴⁵ Overseas Direct Purchases of Tax-exempt Nicotine Solutions Skyrocketed Last Year. The Korea Bizwire. Published October 16, 2020. Available at koreabizwire.com/overseas-direct-purchases-of-tax-exempt-nicotine-solutions-skyrocketed-last-year/172035.

well be that these vendors interpreted the product “tobacco-free” labeling as not relevant to their tobacco policy.

Amazon, eBay, Google Shopping, and Target all publish clearly articulated bans on the sale of tobacco products.^{46,47,48,49} While Walmart sells cigarettes in retail settings, it sustains a policy against online sales. Online stores have differing business models. Google Shopping and e-Bay are marketplaces that primarily connect buyers with sellers. Other vendors sell direct to customers, feature paid advertisements linked to third-party vendors, or both. For example, Amazon sold nicotine pouches 2ONE and RUSH via Amazon Prime while it sold Lucy via advertisements with links to the brand website. We also evaluated major national chain pharmacies (e.g., CVS, Walgreens, Rite Aid) and found that they did not sell or allow pop up advertisements for either TFN or SYN products, only FDA authorized nicotine replacement products.

Tobacco-Free Nicotine: Sold By Online Retailers Which Prohibit Tobacco Products

Google Shopping amazon.com TARGET ebay

Google Shopping				amazon.com					TARGET					ebay				
 <p>Nicotine Toothpick Flavor Bundle Pack (60 Nicotine...)</p> <p>\$14.99 Zipix Free shipping</p>	 <p>on! 8mg Coffee</p> <p>\$2.49 Northerner Free shipping</p>	 <p>Velo Max Pouch Dragon Fruit 7MG</p> <p>\$3.99 Northerner Free shipping</p>	 <p>Mint-Melon Nicotine Toothpicks (20 Count Nicotine...)</p> <p>\$5.99 Zipix Free shipping</p>	 <p>ZYN Menthol 3MG Nicotine Pouches</p> <p>\$3.79 Northerner Free shipping</p>	 <p>Wintergreen Pouches 2-Pack</p> <p>\$12.00 Black Buffalo</p>	 <p>Smooth Peach Pouch</p> <p>\$35.88 BaccOff</p>	 <p>Lucy 4mg Strength Nicotine Gum (3 Pack Trial)</p> <p>\$5.00 lucy.co Free shipping</p>	 <p>FRE Mint 12MG Nicotine Pouches</p> <p>\$3.99 Northerner Free shipping</p>										
 <p>on! 2mg Original</p> <p>\$2.49 Northerner Free shipping</p>	 <p>Rogue Nicotine Pouches - Wintergreen - 3mg...</p> <p>\$5.29 Altfree</p>	 <p>BaccOff Classic Apple Blend Pouch Roll (12 Cans) - An...</p> <p>\$35.88 BaccOff</p>	 <p>Fully Loaded Chew: Cherry Flavor - 50% Nicotine Strength...</p> <p>\$21.99 Fully Loaded Chew</p>	 <p>NIC-S Fresh Mint 6MG Nicotine Pouches</p> <p>\$3.99 Northerner Free shipping</p>	 <p>NIC-S Spiced Cinnamon 9MG Nicotine Pouches</p> <p>\$3.99 Northerner Free shipping</p>	 <p>Velo Pouch Cinnamon 4MG</p> <p>\$3.99 Northerner Free shipping</p>	 <p>on! Nicotine Pouches - Citrus - 4mg - 20 Pouches</p> <p>\$4.69 Altfree</p>	 <p>NIC-S Sweet Orange 9MG Nicotine Pouches</p> <p>\$3.99 Northerner Free shipping</p>	 <p>Velo Nicotine Pouches - Mint - 4mg - 15 Pouches</p> <p>\$5.29 Altfree</p>									

⁴⁶ Amazon policy on prohibited products. <https://advertising.amazon.com/resources/ad-policy/sponsored-ads-policies>

⁴⁷ eBay policy on prohibited and restricted items. <https://www.ebay.com/help/policies/prohibited-restricted-items/prohibited-restricted-items?id=4207>.

⁴⁸ Google Shopping Tobacco Policy. <https://support.google.com/merchants/answer/6150004?hl=en>

⁴⁹ Walmart Marketplace prohibited products policy. <https://www.walmart.com/help/article/marketplace-prohibited-products-policy/94d99d15c54049e19c5c0192facafadb>

Tobacco-free and synthetic nicotine products offered for sale on major online shopping sites (August 2021). None of these vendors offer cigarettes, cigars, e-cigarettes, e-liquids, or other tobacco products online. Among the three brick-and-mortar stores, only Target does not sell tobacco products (since 1996) while Kmart and Walmart continue to do so.

	Amazon	eBay	Google Shopping	Kmart	Target	Walmart
Product Listings	2One (Amazon Prime) Lucy* Rush (Amazon Prime)*	2One Lucy Rogue Velo	Black Buffalo* Fre ^{2*} Lucy* Nic-S ^{2*} Nicotine Picks* Niin* On! ^{2*} Pixotine* Rogue* Smart Toothpicks Velo ^{2*} White Fox ^{2*} Whitetail ^{2*} Zippix * Zyn ^{2*}	Black Buffalo* Fre ^{2*} Lucy* Nicotine Picks* On! ^{3*} Pixotine* Solace ^{2*} Zippix* Zyn ^{2*}	Black Buffalo* Fre ^{2*} Lucy* Nicotine Picks* Niin* On! ^{3*} Pixotine* Rogue ^{2*} Solace ^{2*} Velo ^{2*} Zippix* Zyn ^{2*}	2One ³

¹ Direct link to brand website if no notation

²Third Party vendors (e.g. Nicokick.com, Altfree.com, Northerner.com)

*The product appears in a sponsored ad.

FDA Orders Halt in Sales – Sales Resume with Reformulated with Synthetic Nicotine

In July 2020, the FDA ordered disposable e-cigarette brand Puff Bar to cease its sales as it had not been authorized to be on the market.⁵⁰ Puff Bar resumed sales in February 2021 claiming that it was now formulated with TFN and was thus exempt from FDA tobacco regulations.^{51 52 53} In August 2020, the FDA issued a market denial order (MDO) to a series of e-cigarette companies, including Vapor Salon.⁵⁴ The next day, Vapor Salon announced it was switching to TFN and

⁵⁰ US Food and Drug Administration. FDA Notifies Companies, Including Puff Bar, to Remove Flavored Disposable E-Cigarettes and Youth-Appealing E-Liquids from Market for Not Having Required Authorization. July 20, 2020. <https://www.fda.gov/news-events/press-announcements/fda-notifies-companies-including-puff-bar-remove-flavored-disposable-e-cigarettes-and-youth>

⁵¹ Maloney J. Puff Bar Defies FDA Crackdown on Fruity E-Cigarettes by Ditching the Tobacco. Wall Street Journal. March 2, 2021. <https://www.wsj.com/articles/puff-bar-defies-fda-crackdown-on-fruity-e-cigarettes-by-ditching-the-tobacco-11614681003>.

⁵² Ramamurthi, D., Chau, C., Berke, H.Y., Tolba, A.M., Yuan, L., Kanchan, V., Santos, G. and Jackler, R.K., 2022. Flavour spectrum of the Puff family of disposable e-cigarettes. *Tobacco control*. <https://tobaccocontrol.bmj.com/content/early/2022/01/10/tobaccocontrol-2021-056780>

⁵³ CBS Morning. How companies like Puff Bar have avoided FDA regulation: "The industry can innovate around it" December 15, 2021. <https://www.cbsnews.com/news/puff-bar-fda-regulation-loopholes/>

⁵⁴ US Food and Drug Administration. FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health. FDA Announcement. August 26, 2021.

claimed it could once again market any flavors it wanted.⁵⁵ A series of companies have filed appeals to PMTA MDO orders.⁵⁶ Some have succeeded in obtaining judicial stays of their MDO.⁵⁷




<https://www.fda.gov/news-events/press-announcements/fda-denies-marketing-applications-about-55000-flavored-e-cigarette-products-failing-provide-evidence>.

⁵⁵ Norcia A. Denied FDA Authorization, Vaping Companies Start to Explore Loopholes. Filter. August 30, 2021. <https://filtermag.org/fda-vaping-marketing-synthetic-nicotine/>.

⁵⁶ McDonald J. Vape company MDO appeals and legal action. February 22, 2022. Vaping 360. (<https://vaping360.com/vape-news/111563/vape-companies-challenging-fda-marketing-denials/>)

⁵⁷ Norcia A. Court Lets Four FDA-Denied Vape Companies Resume Sales, for Now. Filter. February 4, 2022. (<https://filtermag.org/fda-court-bidi-stay/>)



Notes from the Field: E-Cigarette Use Among Middle and High School Students — National Youth Tobacco Survey, United States, 2021


Weekly / October 1, 2021 / 70(39);1387–1389

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2021 NYTS


Puff Bar #1 Among US High School & Middle School Students

2.06 million youths estimated to be current e-cigarette users



High School
26.1%↑

Middle School
30.3% ↑



High School
5.7%↓

Middle School
12.5%↓

https://www.cdc.gov/mmwr/volumes/70/wr/mm7039a4.htm?s_cid=mm7039a4_w

Puff Bar Ordered Off US Market by the FDA in July 2020



FDA Notifies Companies, Including Puff Bar, to Remove Flavored Disposable E-Cigarettes and Youth-Appealing E-Liquids from Market for Not Having Required Authorization

Companies Cited for Marketing Unauthorized Tobacco Products Based on Continued Internet Surveillance During COVID-19 Pandemic

For Immediate Release: July 20, 2020

Puff Bar Relunched February 2021 with “Tobacco-Free Nicotine”

<https://www.fda.gov/news-events/press-announcements/fda-notifies-companies-including-puff-bar-remove-flavored-disposable-e-cigarettes-and-youth>



Underage Sales of “Tobacco-Free” Nicotine via Brand Websites and Online Stores

In the US tobacco product cannot be legally sold to individuals under the age of 21. To test the age restriction for purchase of TFN/SYN brands, in August 2021 we carried by online vendors our synthetic 14-year old boy (Joe Srita) signed up as a customer using his birth date of January 1, 2007, and purchased using either the vendor’s or VISA gift card. In this manner, we evaluated all the TFN/SYN brands sold by online stores for underage sales. Sale was attempted in two ways: via the online store and directly from the brand’s website. Four brand websites enabled underage sale: 2One pouches, Lucy Gum, as well as Zippix and Nicotine Picks toothpicks. Each of the six online vendors sold TFN/SYN to our teenager, with Lucy Gum and 2One pouches most common. Products of two major tobacco companies Velo (RJ Reynolds) and Rogue (Swisher Sweets) were sold via eBay. The only seller in this study which requested age verification was one eBay third party vendor who asked our 14-year-old for age verification and, when no response was forthcoming, shipped the product anyway. It is relevant that US law (the Prevent All Cigarette Trafficking commonly known as the PACT Act) prohibits shipping of all tobacco products, including SYN/TFN, by the US Postal Service (USPS).⁵⁸ All of the products shipped to our underage buyer were shipped via the USPS.

Underage Sales of Nicotine Replacement Products via Online Stores

Both recreational nicotine gums (e.g. Lucy, Rogue, Solace) and those authorized by the FDA for smoking cessation (e.g. Nicorette) are marketed in youth appealing flavors. Therapeutic

⁵⁸ Chowdhury A. Congress Amends the PACT Act to Apply to All Vaping Products, Placing Huge Burden on Small Manufacturers as Third-Party Common Carriers Refuse to Ship Products. National Law Review. 2021; 199. February 4, 2021. (<https://www.natlawreview.com/article/congress-amends-pact-act-to-apply-to-all-vaping-products-placing-huge-burden-small>)

nicotine is widely sold in pharmacies and available via major online vendors. By federal law nicotine for tobacco cessation is not for sale to minors, a regulation which is poorly enforced.⁵⁹ Because teens seeking sweet or fruity sources of nicotine might turn to over the counter therapeutic nicotine products, we tested the online age verification system. Use of nicotine chewing gums has been observed in JUUL addicted teenagers while in school.⁶⁰ In both cases attempted, our 14-year-old was able to purchase Nicorette gum via Amazon.com without any age verification.

US Federal Laws Addressing Non-Tobacco Sourced Nicotine: PACT ACT

In the US Congress, a bill (H.R. 2339) passed the House in February 2020 which expanded the definition of a tobacco product to include synthetic nicotine, but the bill died when it was not acted upon by the Senate. The proposed legislative language was comprehensive: “The term “alternative nicotine” means nicotine that is not made or derived from tobacco plants and may include nicotine that is chemically synthesized, synthesized from recombinant genetic technology, or extracted from non-tobacco plants.”⁶¹ The 2021 PACT Act Amendment, which added additional restrictions on the shipping of tobacco products via the US Postal Service (USPS) (effective March 27, 2021), specifically encompassed: “all forms of nicotine, whether natural or synthetic in origin.”^{62 63} That numerous SYN and TFN products were shipped to us by the USPS as part of this study (July 2021 – February 2022) indicates that compliance with the PACT is inconsistent. Samples of SYN and TFN products shipped to us via the USPS included disposable e-cigarettes (Puff Bar, Ignite), e-liquids (Air Factory), pouches (2ONE, RUSH, Velo, Lucy), toothpicks (NicotinePicks, Zippix), and gums (Lucy, Rogue).

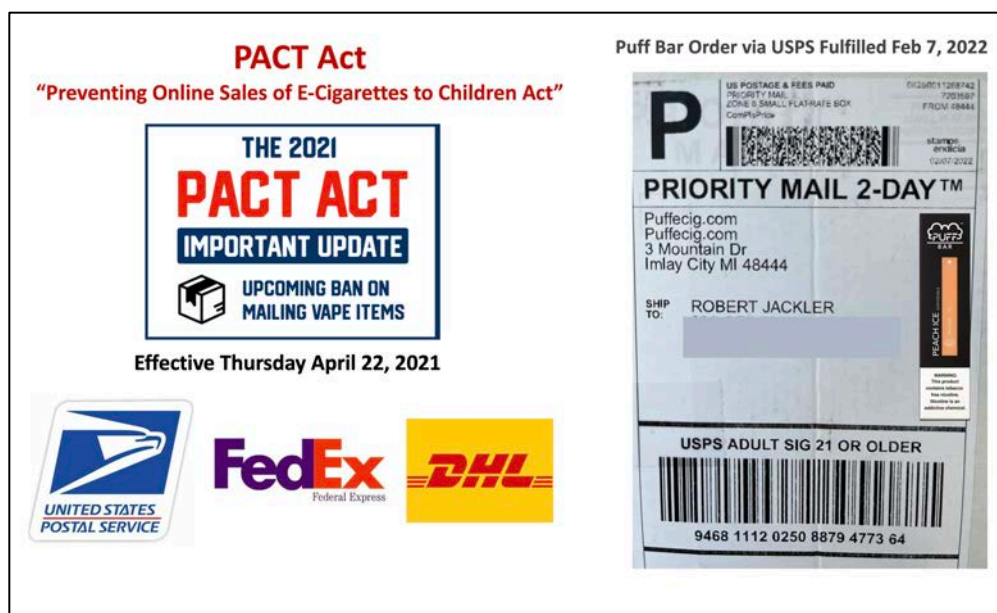
⁵⁹ Johnson KC, Klesges LM, Somes GW, Coday MC, DeBon M. Access of Over-the-counter Nicotine Replacement Therapy Products to Minors. *Arch Pediatr Adolesc Med.* 2004;158(3):212–216. doi:10.1001/archpedi.158.3.212

⁶⁰ Reader R. Juul-addicted teens are chewing nicotine gum just to get through school. *Fast Company.* December 19, 2019. <https://www.fastcompany.com/90444747/juul-addicted-teens-are-chewing-nicotine-gum-just-to-get-through-school>

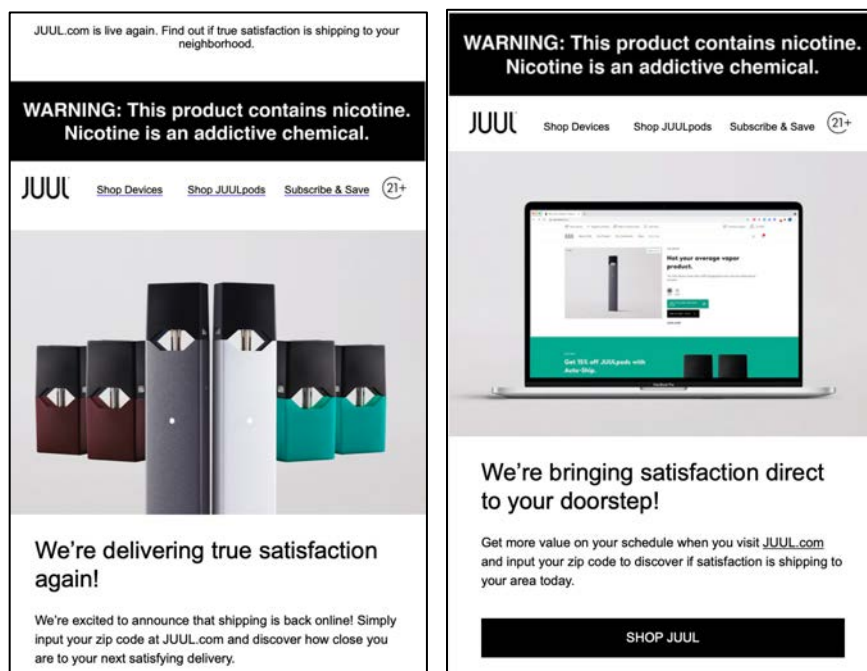
⁶¹ US Congress. H.R.2339 - Protecting American Lungs and Reversing the Youth Tobacco Epidemic Act of 2020. <https://www.congress.gov/bill/116th-congress/house-bill/2339/text>.

⁶² The 2020 PACT Act. Treatment of E-Cigarettes in the Mail. Published October 21, 2021. <https://www.govinfo.gov/content/pkg/FR-2021-10-21/pdf/2021-22787.pdf>.

⁶³ The 2020 PACT Act amendment, the “Preventing Online Sales of E-Cigarettes to Children Act. <https://www.congress.gov/bill/116th-congress/senate-bill/1253>



Private shippers including FedEx, DHL, and the United Parcel Service (UPS) aligned their policies with the PACT Act and prohibit shipping of all tobacco products.⁶⁴ ⁶⁵ Smaller shippers have filled the void and advertise to the tobacco industry their willingness to ship their product.⁶⁶



e-Mails from JUUL to customers (May 11 & June 8, 2021) announcing resumption of shipping.

⁶⁴ UPS, DHL, and FedEx join USPS in vape mail ban. Freight Right. March 29, 2021. <https://www.freightright.com/news/vape-mail-ban>

⁶⁵ FEDEX policy prohibiting shipping of all tobacco product. <https://www.fedex.com/en-us/shipping/guidelines-for-shipping-tobacco.html>

⁶⁶ How To Ship Vapes Despite The PACT Act. Easyship. <https://www.easyship.com/blog/ship-vapes-pact-act>

DISCUSSION

After centuries of selective cultivation, commercial tobacco plants are highly efficient in producing abundant nicotine which can be extracted economically and marketed as a bulk chemical product. While extracting nicotine from tobacco leaf is efficient and inexpensive, synthesis from precursor compounds is relatively complex and expensive. A series of patents have appeared in recent years describing various methods of synthesizing nicotine from non-tobacco precursor products. NGL’s patent for its TFN[®] product is noteworthy due to its market leadership.⁶⁷

In 2013, e-cigarette Greensmart living advertised that it was “100% tobacco free” with nicotine derived from “non-tobacco plant sources.”⁶⁸ This was almost certainly not a valid claim.



In 2016 HiLIQ NTN claimed to offer “pure & clean” non-tobacco nicotine which analysis by a competitor (NGL) found to be tobacco derived.^{69,70} Similarly, in 2020 NGL warned of “fake and counterfeit” SYN products being offered by Chinese manufacturers.⁷¹ While synthetic nicotine market leader NGL repeatedly issues press releases accusing competitors of unethical business

⁶⁷ NextGenerationLabs LLC. Nicotine composition for vaping devices. US Patent 2017/0112182 A1. Accessed December 11, 2021.

⁶⁸ E-cig company, GreenSmartLiving, unveils new packaging, slogan. GreenSmartLiving takes a unique stance in the electronic cigarette market. Cision PR Wire. July 2, 2013. <https://www.prnewswire.com/news-releases/e-cig-company-greensmartliving-unveils-new-packaging-slogan-214014211.html>

⁶⁹ NTN – A New Generation of Nicotine. <https://blog.hiliq.com/ntn-a-new-generation-of-nicotine/>.

⁷⁰ Authenticity Case Study HiLiQ –NTN “Non Tobacco Nicotine. NextGenerationLabs. https://www.dropbox.com/sh/hjeic43setqq5t9/AABTIFOHq8qDhadDSXc0CEKra/Nicotine/Pure%20Nicotine/TFN/General%20Documents?dl=0&preview=1-NGL_HiLiQ_authenticity_Report_FINAL.pdf&subfolder_nav_tracking=1.

⁷¹ Next Generation Labs warns of surge in fake and counterfeit synthetic nicotine products coming from China. PR Wire. Published September 17, 2020. https://www.prweb.com/releases/next_generation_labs_warns_of_surge_in_fake_and_counterfeit_synthetic_nicotine_vape_products_coming_from_china/prweb17398859.htm.

practices, the company’s co-founder was sentenced to 2 years in prison in 2018 for embezzlement of \$833,000 from a tobacco trade group.^{72 73 74}

In the US, nicotine addiction warnings are mandated by the FDA with precise language and formatting requirements.⁷⁵ While these may not technically apply to SYN products, quite a few brands alter these required warnings by inserting terms such as “tobacco-free,” “not tobacco derived,” or “tobacco-leaf free” including some using TDN.

Marketing claims assert that SYN and TFN products have improved taste and aroma compared with TDN brands. As innumerable sweet and fruity nicotine products thrive on the market using TDN, this is unlikely to be an important differentiator. Rather, arguments of improved taste are being used as justifications to deflect from the actual reason for SYN/TFN adoption, which is regulatory escape.⁷⁶ SYN and TFN also convey a message of healthfulness communicated by descriptors such as “clean” and “pure.” The inclusion of the word “free” suggests freedom from harm.⁷⁷ Among youth, many believe that the nicotine in e-cigarettes is “artificial” and express the belief that that means it is safer.⁷⁸ The marketing messages also seek to liberate their products from the stigma of tobacco and portray them as an advanced and more modern alternative.

Our study reveals that tactic of using TFN and SYN to escape limitations extends well beyond governmental regulations. Major online retailers which prohibit sales of tobacco products on their platforms offer TFN and SYN products for sale and even permit paid advertising. Similar widespread sales via online vendors (eBay) have been noted for JUUL.⁷⁹ As other categories of tobacco products (e.g. cigarettes, cigars) were not sold or promoted via these channels, it appears that screening tools used by these vendors may be bypassed by the “tobacco-free” description. Underage sales of SYN/TFN products by major online retailers is concerning and necessitates action by both the merchants and regulators.

⁷² Synthetic nic entrepreneur Ron Tully charged with mail fraud. Vaping 360. October 5, 2017. <https://vaping360.com/vape-news/56916/ron-tully-mail-fraud/>.

⁷³ Tully Pleads Guilty in \$833,000 Mail Fraud. Tobacco Business. October 23, 2017. <https://tobaccobusiness.com/ronald-tully-pleads-guilty-in-833000-mail-fraud/>

⁷⁴ Green F. Richmond Times Dispatch. Co-Founder of Richmond-Based trade association sentenced in 833,000 mail fraud case. Sentenced to 2 years. January 10, 2018. https://richmond.com/news/local/crime/co-founder-of-richmond-based-trade-association-sentenced-in-833-000-mail-fraud-case/article_d88bd937-493f-59fe-a03e-4ef51aa97b6f.html

⁷⁵ US Food and Drug Administration. Covered Tobacco Products and Roll-Your-Own/ Cigarette Tobacco Labeling and Warning Statement Requirements. FDA. October 6, 2020. <https://www.fda.gov/tobacco-products/labeling-and-warning-statements-tobacco-products/covered-tobacco-products-and-roll-your-own-cigarette-tobacco-labeling-and-warning-statement#warning>

⁷⁶ CBS Mornings. Puff Bar CEOs on the company behind the popular e-cigarette brand: "There was a lot of shadowiness before. November 19, 2021. <https://www.cbsnews.com/news/puff-bar-e-cigarette-ceos-fda/>.

⁷⁷ Chen-Sankey J, Ganz O, Seidenberg A, Choi K. Effect of a ‘tobacco-free nicotine’ claim on intentions and perceptions of Puff Bar e-cigarette use among non-tobacco-using young adults. *Tob Control*. 2021. PMID: 34697090

⁷⁸ Pepper JK, Farrelly MC, Watson KA. Adolescents' understanding and use of nicotine in e-cigarettes. *Addict Behav*. 2018;82:109-113.

⁷⁹ Laestadius L, Wang Y. Youth access to JUUL online: eBay sales of JUUL prior to and following FDA action. *Tob Control*. 2019;28:617-622.

The importance of clarity in product definitions in describing tobacco products in legislation and regulation has been emphasized.⁸⁰ Ambiguities have long been exploited by the tobacco industry that has often lobbied to adopt “Trojan horse” terms and definitions which enable escape from regulatory efforts. While the Congressionally mandated FDA definition of a tobacco product clearly specifies origin from the plant, the Agency’s guidance is more nuanced: “E-liquids that do not contain nicotine or other substances made or derived from tobacco may still be components or parts and, therefore, subject to FDA’s tobacco control authorities . . . FDA intends to make these determinations on a case-by-case basis, based on a totality of the circumstances.”⁸¹

FDA statements in 2016 regarding SYN, and also nicotine-free e-cigarettes, contain similar language emphasizing the Agency’s authority over what it terms “constituent parts” under certain circumstances may be considered as tobacco products.^{82,83} Despite pleas from health and advocacy organizations, we are unaware of the FDA having taken action to insist that products claiming to employ SYN or TFN be subject to FDA regulations.⁸⁴ A legal analysis of pathways to close the synthetic nicotine loophole concluded that no rationale exists for exempting such an addictive drug from regulation.⁸⁵ In discussing whether the FDA’s Center for Tobacco Products or its Center for Drug Evaluation and Research (CDER) would be the most appropriate regulatory body, the article recommended classification of SYN as a drug under the definition: “articles (other than food) intended to affect the structure or any function of the body of man or other animals.”⁸⁶

All forms of nicotine, whether derived from tobacco plants or synthetic contain impurities. While residuals from tobacco leaf extraction are well known, byproducts of the chemical synthesis of nicotine have not been characterized for potential human toxicity and carcinogenicity. In addition, synthetic nicotine manufacturers may use different chemical methods and thus product differing byproducts. Justified by concerns for unknown safety risk, the FDA should insist upon toxicity/carcinogenicity studies of synthetic nicotine products before they are marketed.⁸⁷ The

⁸⁰ Lempert LK, Grana R, Glantz SA. The importance of product definitions in US e-cigarette laws and regulations. *Tob Control*. 2016;25:e44-51.

⁸¹ US Food and Drug Administration “Frequently asked questions” reply regarding its policy on synthetic nicotine. <https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/commonly-asked-questions-about-center-tobacco-products#14>

⁸² Sullum J. The FDA Keeps Us Guessing About the Scope of Its E-Cigarette Regulations. *Reason*. December 16, 2016. <https://reason.com/2016/12/16/the-fda-keeps-us-guessing-about-the-scope/>.

⁸³ Sullum J. FDA Says Nicotine-Free E-Liquids Are Tobacco Products in 'Certain Circumstances'. August 19, 2016. <https://reason.com/2016/08/19/fda-will-regulate-nicotine-free-e-liquid/>

⁸⁴ Letter from American Lung Association and six other organization to FDA Acting Commissioner Janet Woodcock. March 18, 2021.A <https://www.lung.org/getmedia/4748ba27-73ba-4271-997d-a363edba78ba/fda-letter-re-puff-bar-synthetic-nicotine-final.pdf>.

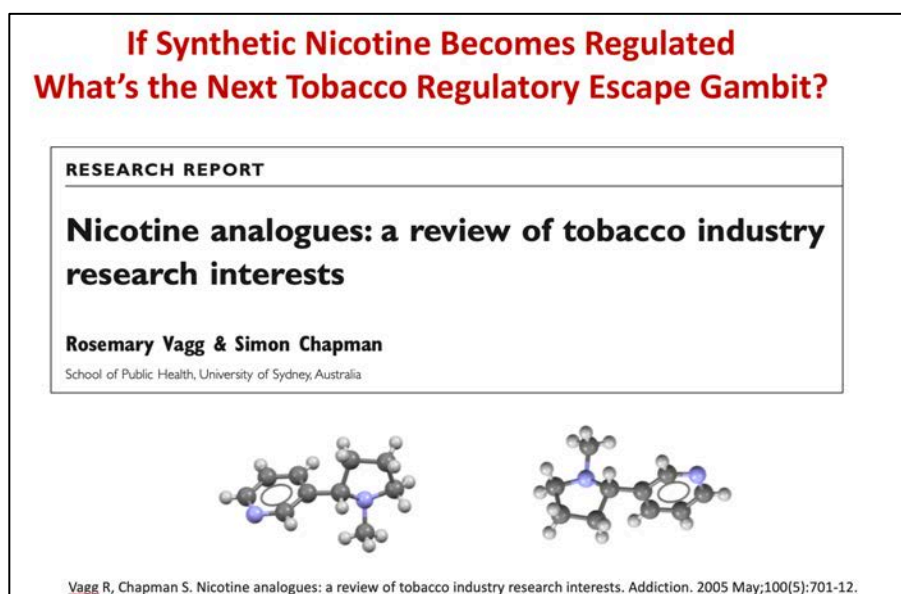
⁸⁵ Zettler PJ, Hemmerich N, Berman ML. Closing the Regulatory Gap for Synthetic Nicotine Products. *Boston Coll Law Rev*. 2018;59:1933-1982.

⁸⁶ United States Code 21 U.S.C. § 321 Unannotated Title 21. Food and Drugs § 321. Definitions; generally. <https://codes.findlaw.com/us/title-21-food-and-drugs/21-usc-sect-321.html>.

⁸⁷ Gupta AK, Mehrotra R. Safety Concerns For Tobacco-Free Products Containing Synthetic Nicotine. *Nicotine Tob Res*. 2021; 23.

FDA should also consider systematic testing of products claiming to be tobacco-free as at least a fraction of brands may actually prove to have chemical signatures indicative of tobacco origin.

Given the resourcefulness of the tobacco industry in escaping the intent of regulation, should government close the SYN loophole using a narrow definition, efforts to circumvent it will likely follow. Internal tobacco industry documents reveal exploration of nicotine analogues as potential substitutes for nicotine as a means of escaping regulation.⁸⁸ Noteworthy is a patent filed by a vaping company in 2014 to extract “imitation nicotine” from betel nuts (areca fruits), which are widely chewed for their stimulant effects in India and Southeast Asia.⁸⁹ Betel nuts contain arecoline, a psychoactive drug with effects similar to nicotine.⁹⁰



Regulatory Implications:

As it is a potentially addictive substance, there is no justification for nicotine, regardless of its source, to be exempt from regulation. The SYN loophole, a regulatory lacuna increasing exploited by brands, is an unintended byproduct of what was thought by its makers to be a comprehensive definition of a tobacco product. In closing this gap, non-tobacco sourced nicotine needs to be designated as either a drug or tobacco product. Empowering the FDA Center for Tobacco Products to regulate non-tobacco sourced nicotine would require an act of Congress. The FDA, however, does appear to have authority to consider non-tobacco sourced nicotine under its existing authority to regulate drugs via CDER. Concern that non-tobacco nicotine products may

⁸⁸ Vagg R, Chapman S. Nicotine analogues: a review of tobacco industry research interests. *Addiction*. 2005;100:701-12.

⁸⁹ Balder E. US patent 9526270 for Vapor Corp. Synthetic or imitation nicotine compositions, processes and methods of manufacture. December 27, 2016. <https://patents.google.com/patent/US9526270B2/en>.

⁹⁰ Papke RL, Horenstein NA, Stokes C. Nicotinic Activity of Arecoline, the Psychoactive Element of "Betel Nuts", Suggests a Basis for Habitual Use and Anti-Inflammatory Activity. *PLoS One*. 2015;10:e0140907.

serve as a gateway to nicotine addiction among adolescents, and its deleterious effects on teen brain development, argue for its categorization as a drug.^{91 92}

Purveyors of SYN and TFN brands claim they are not tobacco products. Logically, if not tobacco, then these products are unapproved drugs and the FDA has existing authority to halt their sales and require them to apply for pre-market authorization. In addition, the Agency would be well justified to prohibit advertising descriptors such as tobacco-free, non-tobacco, zero-tobacco, tobacco-leaf free, clean, pure, and other messaging connoting greater healthfulness absent scientific proof and formal harm reduction designation. Online marketplaces that prohibit tobacco sales should be encouraged to implement their existing corporate policies and, if necessary, update them to specifically exclude all recreational nicotine products. Having received numerous SYN and TFN products shipped via the USPS indicates that the PACT Act compliance is deficient and that its enforcement efforts need to be stepped up.

A fraction of nicotine products claiming to be “tobacco-free” may contain tobacco-sourced nicotine and thus are subject to existing FDA tobacco regulations and tobacco taxation. As the veracity of SYN and TFN claims is suspect in many cases, the Agency should initiate a program of chemical analysis of products described as SYN/TFN to identify tobacco residuals.⁹³ The FDA should also require companies to describe their supply chain, provide detailed disclosure of chemical constituents and synthetic contaminants, and visit manufacturers to inspect their production methods. In October 2017, the FDA created a Nicotine Steering Committee with the purpose of developing and implementing nicotine policy and regulation.⁹⁴ Ideally, this body will put forward a comprehensive regulatory framework encompassing all sources and forms of nicotine.

**“Synthetic” & “Tobacco-Free” Nicotine Products
Escapes from Regulation**

- **FDA Tobacco Regulations**
- **PMTA Requirement (FDA Tobacco Product Authorization)**
- **Tobacco Taxation**
- **USPS Tobacco Shipping Restrictions**
- **Tobacco Sales Bans of Major Online Stores**
- **Underage Sales by Online Vendors**

⁹¹ McGrath- Morroa SA, Gorzkowski J., Groner JA, et al. The Effects of Nicotine on Development. *Pediatrics*. 2020;154(3).

⁹² Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, Yang J, Primack BA, Andrews JA, Miech RA, Spindle TR, Dick DM, Eissenberg T, Hornik RC, Dang R, Sargent JD. Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. *JAMA Pediatr*. 2017 Aug 1;171(8):788-797. doi: 10.1001/jamapediatrics.2017.1488.

⁹³ Jordt SE. Synthetic nicotine has arrived. *Tob Control*. 2021 Sep 7. doi: 10.1136/tobaccocontrol-2021-056626. Epub ahead of print. PMID: 34493630.

⁹⁴ US Food and Drug Administration. FDA Nicotine Steering Committee. <https://www.fda.gov/about-fda/office-clinical-policy-and-programs/nicotine-steering-committee>.

Supplement Search Strategies: Keywords for identifying synthetic and tobacco-free nicotine brands and manufacturers.

Google keyword search terms

Synthetic nicotine brands
Synthetic nicotine vape
Synthetic nicotine vape juice
Synthetic nicotine pouches
Synthetic nicotine disposables
Synthetic nicotine toothpicks
tobacco-free nicotine brands
tobacco-free nicotine vape
tobacco-free nicotine vape juice
tobacco-free nicotine pouches
tobacco-free nicotine disposables
best tobacco-free nicotine brands
best synthetic nicotine brands
synthetic nicotine for sale
tobacco-free nicotine for sale

Identifying online vendors

Best online vape store/stores
Top online vape store
Top vape stores online
Synthetic nicotine online
tobacco-free nicotine online
synthetic nicotine wholesale
synthetic nicotine manufacturers
tobacco-free nicotine wholesale
tobacco-free nicotine manufacturers
Online Vendor Website list
<https://www.electrictobacconist.com/>
<https://www.elementvape.com/>
<https://www.ejuices.com/>
<https://www.eightvape.com/>
<https://www.directvapor.com/>
<https://www.vaporbeast.com/>
<https://vaperoyalty.com/>
<https://www.flawlessvapeshop.com/>
<https://www.giantvapes.com/>
<https://www.vaporfi.com/>
<https://www.vaporaauthority.com/>
<https://vaping.com/>
<https://myvpro.com/>
<https://vapordna.com/>
<https://www.ukecigstore.com/>

Patent and Trademark Databases- searches for “synthetic nicotine”

Google patents (<https://patents.google.com/>)
United States Patents Database (<https://www.uspto.gov/patents>)
United States Trademark Database (<https://www.uspto.gov/trademarks>)