The use of synthetic nicotine in various products including e-cigarettes and nicotine pouches has become more common in recent years. Because synthetic nicotine is relatively new, any unique health risks are still unknown, but regardless of the source, nicotine is highly addictive, can be harmful to adolescent brain development, and is dangerous to pregnant women and their developing babies.

On March 15, 2022, President Biden signed the Consolidated Appropriations Act, 2022, which gave FDA’s Center for Tobacco Products jurisdiction to regulate synthetic nicotine products by amending the tobacco product definition in the 2009 Family Smoking Prevention and Tobacco Control Act to include products “containing nicotine from any source.” This was an important action because companies were taking advantage of policy gaps in federal and state policy and introducing products containing synthetic nicotine come in a variety of flavors and styles that could be highly appealing to youth.

What is Synthetic Nicotine?

Synthetic nicotine is a man-made chemical copy of the nicotine that is extracted from tobacco plants. Nicotine has two forms: the S-nicotine isomer and the R-nicotine isomer. Tobacco-derived nicotine is almost exclusively in the S-nicotine form. Early methods to synthesize nicotine produced an equal mixture of the S-nicotine and R-nicotine, but more recently, manufacturers have developed methods to refine the synthetic mixture to create different ratios of the isomers and even products that are close to all S-nicotine. Once deemed cost prohibitive for widespread use, recent declines in the cost of manufacturing synthetic nicotine has opened the door for more companies to use it.

As early as the 1960s, tobacco companies including British American Tobacco, R.J. Reynolds, and Liggett & Myers, considered using synthetic nicotine to supplement tobacco-derived nicotine in products, not as a replacement. However, the high cost of production and concerns about the isomeric mixture led them to abandon further study of it.

Synthetic nicotine is manufactured and processed in various countries, including India and China. Finished products using synthetic nicotine can be assembled in another location. For instance, many disposable e-cigarettes using synthetic nicotine are made in China, though the source for the synthetic nicotine used in those products is unknown.

Synthetic nicotine is currently being used in e-cigarettes, nicotine pouches, and traditional “moist snuff” products. Some companies offer both tobacco-derived and synthetic varieties of their nicotine e-liquids, using the same brand and same or similar flavors. Some examples of products made with synthetic nicotine include disposable e-cigarette Puff Bar, NIIN nicotine pouches, and Fully Loaded Chew “moist snuff.”

These products are available in a wide variety of flavors and nicotine levels. Online, the Puff Bar website currently advertises three disposable e-cigarette devices in nearly two dozen flavors, including Strawberry Banana, Cool Mint, Watermelon, Blue Razz, Mango, Passionfruit and Lemon Ice. Other e-cigarette retailers sell synthetic nicotine e-liquids in an array of kid-friendly flavors, including Pink Lemonade, Kookie Krunch, and Blue Slushee. Similarly, synthetic nicotine pouches are available in flavors such as sweet and raspberry lemonade mint, while “moist snuff” products are available in flavor such as mint and cherry.

While synthetic nicotine has gained a lot of attention, the vast majority of products containing nicotine on the U.S. market continue to use tobacco-derived nicotine.
Public Health Concerns

Because products containing synthetic nicotine are relatively new, data on any unique health risks are not yet available, but nicotine itself has known health risks. CDC researchers recently warned, “Whether derived from tobacco plants or synthetically developed in a laboratory, nicotine is an addictive drug with known adverse health consequences. Nicotine harms fetal development and use during adolescence can cause addiction and can harm parts of the brain that control attention, learning, memory, mood, and impulse control. Nicotine use may also increase adolescents’ risk of future addiction to other drugs.”\(^{11}\)

It is currently unknown if there are any differences between the health effects of using products made with synthetic or tobacco-derived nicotine. While animal studies have indicated that the R-nicotine form has similar but less potent pharmacological effects compared to the S-nicotine form,\(^{12}\) it is unclear how the presence of R-nicotine at various ratios in mixtures may impact the addictive or harm potential of products on humans.

Youth Use. Although national data on use of products with synthetic nicotine are not available, there are some indications that youth are using them. In 2022, 14% of high school e-cigarette users and 17.7% of middle school e-cigarette users reported Puff Bar as their preferred e-cigarette brand, making it the most popular e-cigarette brand among both middle and high schoolers.\(^{13}\) Puff Bar announced that it was using synthetic nicotine in its products in February 2021.

CDC researchers stated, “Introduction of synthetic, flavored nicotine products that fall outside of existing statutory definitions of tobacco products may undermine existing efforts to reduce youth tobacco product use and to support youth tobacco cessation.”\(^{14}\)

Marketing and Claims

Many companies are marketing synthetic nicotine using various claims about its quality or characteristics compared to traditional tobacco-derived nicotine, such as “pure,” or “odorless,” while some marketing does not differentiate between synthetic nicotine or tobacco-derived nicotine at all. Currently no independent or government agency has verified the quality of these products or the validity of these claims.

- Puff Bar states that its products are made with “a virtually tasteless, odorless, nicotine without the residual impurities of tobacco-derived nicotine.”\(^{15}\)
- NGL, producer of the synthetic nicotine brand “Tobacco-Free Nicotine” (TFN), has stated that “TFN is devoid of many of the residual impurities that tobacco derived nicotine contains… TFN is virtually tasteless and odorless… there is no need to mask the off-flavor and aroma of tobacco-based nicotine.”\(^{16}\) Many companies use TFN in their e-liquids or pouches.
- NIIN, a company that produces oral nicotine products, claims its products are “completely free of many residuals and constituent impurities that are commonly found in tobacco-derived nicotine.”\(^{17}\)

Perhaps to avoid regulation as a drug product, some companies carefully avoid using therapeutic or health-related terms in their advertising. In a press statement about the launch of its ZIA nicotine gum, NGL described the product as “a recreational synthetic nicotine alternative to cigarettes, vape products and other forms [of] tobacco products” and “highly satisfying.”\(^{18}\)

Other companies are more brazen in their claims. NIIN sponsored an article in Newsweek that stated, “Enjoy the Calming Effects of Nicotine Without the Health Risks of Tobacco Smoke,” and though it did not explicitly tell readers to use NIIN pouches to stop smoking, the paid article made statements about quitting smoking (“If you’ve been trying to quit smoking for a while, you know first-hand how hard it can be, and how important small changes can be.”) and the dangers of smoking, which it then contrasted with
positive statements about NIIN’s synthetic nicotine pouches: “Additionally, tobacco smoke can trigger an asthma attack or make an attack worse, according to the CDC. Many are turning to tobacco-free alternatives that still provide the effects of nicotine.”

Some companies have marketed products made with tobacco-derived nicotine and others with synthetic nicotine simultaneously, and in some cases, it can be difficult to differentiate between the two versions. For instance, some online retailers are selling the same brand of e-liquid using tobacco-derived and synthetic nicotine in the same flavors, with very little changes in the packaging to denote the different sources of nicotine.

Companies often described synthetic nicotine as “tobacco-free nicotine,” either specifically referencing the TFN-brand synthetic nicotine or referencing synthetic nicotine more generally. This may cause consumer confusion because some other products described by manufacturers as “tobacco-free,” such as Velo and Zyn, use nicotine derived from tobacco but do not contain tobacco leaf.

While most companies note the nicotine level on their synthetic nicotine products, the ratio of R-nicotine and S-nicotine in the mixture, if relevant, is not specified. For instance, one study found that a synthetic nicotine e-liquid contained twice the amount of nicotine listed on the label, representing only the quantity of S-nicotine not the R-nicotine, while the labels of other tested products listed the total nicotine including both R- and S-nicotine. Consumers may not realize the amount – or types – of nicotine in the products due to a lack of regulation and standards mandating that companies provide clear information.

**Regulation of Synthetic Nicotine**

Starting April 14, 2022, synthetic nicotine products will be regulated as tobacco products by the FDA. This action was urgent and necessary, as one financial analyst group stated, synthetic nicotine “may be a golden ticket: no FDA regulation, no tobacco taxes, no flavor restrictions, and no restrictions on direct to consumer e-commerce.” Falling within a regulatory loophole, these products enjoyed a market advantage over FDA-regulated tobacco-derived nicotine products before the new law took effect. However, they may not be subject to some state or local policies depending on state definitions.

Prior to the new law, synthetic nicotine products were not subject to FDA’s tobacco product regulations because the nicotine was not “derived from tobacco,” which was how tobacco products were originally defined. Now that Congress has given FDA’s Center for Tobacco Products (CTP) the authority to oversee synthetic nicotine products by changing that definition, all of the provisions that cover tobacco products also apply to products using synthetic nicotine. This includes requiring all products made with synthetic nicotine to go through the premarket review process. Since July 13, 2022, synthetic nicotine tobacco products without a marketing order from FDA have been illegal. No synthetic nicotine product has received a marketing order so far, and though FDA has issued refuse-to-accept decisions for some applications and warning letters to some companies for continuing to market products without such order, the market continues to be flooded with these illegal products.

States and localities also need to act to ensure that tobacco control policies cover synthetic nicotine products, by broaden their definitions of tobacco products to include products containing or derived from nicotine, regardless of whether or not the nicotine is derived from tobacco. For example, Massachusetts expanded its tobacco product definition to include “a product containing, made, or derived from tobacco or nicotine that is intended for human consumption.”

*Campaign for Tobacco-Free Kids, October 14, 2022*
1 Jordt, SE, “Synthetic nicotine has arrived.” Tobacco Control, Published Online First, September 7, 2021, doi: 10.1136/tobaccocontrol-2021-056626.
2 Jordt, SE, “Synthetic nicotine has arrived.” Tobacco Control, Published Online First, September 7, 2021, doi: 10.1136/tobaccocontrol-2021-056626.
9 Juice Head website, accessed October 14, 2022 at https://juicehead.co/collections/juice-head-pouches.
12 Jordt, SE, “Synthetic nicotine has arrived.” Tobacco Control, Published Online First, September 7, 2021, doi: 10.1136/tobaccocontrol-2021-056626.