

September 28, 2015

Stephen Ostroff, M.D., Commissioner C/O Division of Dockets Management HFA-305 Food and Drug Administration 5630 Fishers Lane, Room 1061 Rockville, MD 20852

Re: Nicotine Exposure Warnings and Child-Resistant Packaging for Liquid Nicotine, Nicotine-Containing E-Liquid(s), and Other Tobacco Products

Docket No. FDA-2015-N-1514

Dear Commissioner Ostroff:

The Tobacco Control Legal Consortium is pleased to submit these comments to the U.S. Food and Drug Administration (FDA) regarding the protection of the public from the dangers of nicotine poisoning. The Tobacco Control Legal Consortium is a national network of nonprofit legal centers providing technical assistance to public officials, health professionals, and advocates concerning legal issues related to tobacco and public health.¹

¹ The affiliated legal centers include ChangeLab Solutions in Oakland, California; the Legal Resource Center for Tobacco Regulation, Litigation & Advocacy at the University of Maryland School of Law in Baltimore, Maryland; the Tobacco Control Resource Center, a project of the Public Health Advocacy Institute at Northeastern University School of Law in Boston, Massachusetts; the Smoke-Free Environments Law Project at the Center for Social Gerontology in Ann Arbor, Michigan; the Public Health Law Center at the William Mitchell College of Law in

The continuing rise in the popularity of e-cigarettes has led to a corresponding rise in the availability of poisonous nicotine in lethal quantities, accessible in a form that can be easily ingested by infants and children. It should come as no surprise that reports of liquid nicotine poisoning have skyrocketed over the last several years. In the face of a lack of federal oversight, many states have begun to step in and mandate child-resistant packaging to combat this growing public health hazard. With a vast majority of states yet to act and the FDA's comprehensive regulatory authority over tobacco products, the agency must act quickly to prevent any further public health damage from nicotine poisoning.

I. The Public Health Standard in the Family Smoking Prevention and Tobacco Control Act provides the FDA with the authority to mandate child-resistant packaging for products that contain nicotine in liquid, gel, or other easily ingestible forms.

The Tobacco Control Act established a public health standard of review, entirely different from the FDA's traditional "safe and effective" standard to evaluate drugs and medical devices.² In establishing new tobacco product regulations, Congress requires the FDA to conclude that a regulation is "appropriate for the protection of public health." This requirement is framed in terms of "risks and benefits to the population as a whole" including both "users and nonusers" of tobacco products as well as the "increased or decreased likelihood" of tobacco product cessation or initiation.³ Congress intended this new "public health standard" to be a "flexible standard that focuses on the overall goal of reducing the number of individuals who die or are harmed by tobacco products."⁴ Of particular note in this circumstance is the Act's inclusion of both users and nonusers of tobacco products in the calculation of a given action's impact on public health. It is important for the agency to consider the potential danger to those nonusers of e-cigarettes, especially the most vulnerable, who may be poisoned by liquid nicotine in the absence of a requirement to sell the product in child-resistant packaging.

There is no question that once the FDA's regulation deeming e-cigarettes, cigars, and other currently unregulated tobacco products to be within the agency's regulatory jurisdiction, it will be within the FDA's power to require child-resistant packaging for all dangerous, poisonous products that contain liquid nicotine. Upon the finalization of this regulation, it will be the FDA's responsibility to combat nicotine poisoning and the agency must act quickly to do so. There is a clear and present danger and thus, there is no cause for delay.

II. The rise in nicotine poisoning is a public health disaster that warrants swift and appropriate action.

Saint Paul, Minnesota; the Tobacco Control Policy and Legal Resource Center at New Jersey GASP in Summit, New Jersey; and the Center for Public Health and Tobacco Policy in Boston, Massachusetts. ² H.R. REP. NO. 111-58, pt. 1, at 39 (2009), reprinted in 2009 U.S.C.C.A.N. 468, 488,

http://www.gpo.gov/fdsys/pkg/CRPT-111hrpt58/pdf/CRPT-111hrpt58-pt1.pdf.

³ Family Smoking Prevention and Tobacco Control Act, § 906(d)(1), 123 Stat. at 1796 (codified at 21 U.S.C. § 387f(d)(1)) [hereinafter Tobacco Control Act]; see also Tobacco

Control Act, §907(a)(3)(B)(i)(I)-(III), 123 Stat. at 1800 (codified at 21 U.S.C. § 387g(a)(3)(B)(i)(I)-(III)).

⁴ H.R. REP. NO. 111-58, pt. 1, at 39 (2009), reprinted in 2009 U.S.C.C.A.N. 468, 488, http://www.gpo.gov/fdsys/pkg/CRPT-111hrpt58/pdf/CRPT-111hrpt58-pt1.pdf.

E-cigarette use is rapidly rising in the United States. Current use among adults more than doubled between 2010 and 2013 (increasing from 1.0% to 2.6%)⁵ and more recent online polling estimates the current prevalence of e-cigarette use at roughly 10% of U.S. adults.⁶ E-cigarette use has become even more pervasive among younger populations. Between 2013 and 2014, e-cigarette use by high school students more than tripled (from 4.5% to 13.4%). With this increase, e-cigarettes are now the most popular tobacco product among high school students, with over 2 million high school students using them.⁷

The growing prevalence of e-cigarette use increases the likelihood of exposure to large quantities of highly concentrated nicotine among children and adults. The nicotine in e-cigarettes is administered in liquid form and is readily available for purchase in plastic or glass bottles that hold between 15 to 30 milliliters (ml). Consumers are able to choose the concentration of nicotine in their liquid typically ranging from 0 mg/ml to 24 mg/ml.⁸ A small bottle (15 mg) of a mid to high level dosage of liquid nicotine (18 mg/ml) may contain up to 270 mg of nicotine. Thus, given the size of the bottles and the nicotine concentration of the liquid, the levels of liquid nicotine readily available can put users and those around them at risk for nicotine poisoning.

Exposure to liquid nicotine through oral ingestion (drinking the solution) or transdermal contact (absorbed through the skin) can produce different physiological responses depending on the level of dosage. The dose relationship of nicotine is complex and while low doses typically result in stimulant effects, higher doses can have the effects of a depressant. ⁹ The most common outcomes of exposure to nicotine poisoning are minor effects, including symptoms such as vomiting, nausea, and ocular irritation.¹⁰ However, higher levels of exposure and overdoses of liquid nicotine can cause respiratory failure and, ultimately, death.¹¹ Nicotine is estimated to be lethal at doses between 2.2 and 26.2 mg per pound (lb.) of bodyweight, which means that 1 teaspoon (5 ml) of a 1.8% nicotine solution could be lethal to a 200 lb. person.¹²

While the nicotine content in e-cigarette liquid is potentially lethal for all people, children are particularly vulnerable to accidental poisonings from the liquid nicotine in e-cigarette liquids for two reasons.¹³ First, the lower body weights of young children leave them more vulnerable to

http://www.cdc.gov/media/releases/2015/p0416-e-cigarette-use.html (last visited Aug. 31, 2015).

⁵ Brian King, Roshni Patel, Kimberly Nguyen & Shanta Dube, *Trends in awareness and use of electronic cigarettes among US adults, 2010-2013*, NICOTINE & TOBACCO RES. ntu191 (2014).

⁶ Jilian Mincer, *E-cigarette usage surges in past year: Reuters/Ipsos poll* (Jun.10 2015, 8:09 am),

http://www.reuters.com/article/2015/06/10/us-usa-ecigarette-poll-analysis-idUSKBN00Q0CA20150610. ⁷ E-cigarette use triples among middle and high school students in just one year, CDC.GOV,

⁸M.L Goniewicz, T. Kuma, M. Gawron, J. Knysak, & L. Kosmider, L. *Nicotine levels in electronic cigarettes*, 15(1) NICOTINE & TOBACCO RES. 158-66 (2012).

⁹ Biagio Solarino, Frank Rosenbaum, Benno Rießelmann, Claas T. Buschmann & Michael Tsokos, *Death DUE to ingestion of nicotine-containing solution: Case report and review of the literature*, 195 (1) FORENSIC. SCI. INT'L. e19, e-19-e22 (2009).

¹⁰J. P. Vakkalanka, L. S. Hardison Jr. & C. P. Holstege, *Epidemiological trends in electronic cigarette exposures* reported to US Poison Centers, 52 CLINICAL TOXICOLOGY, 542, 545-546 (2014).

¹¹ Jin Jun, Hyoungjoong Kim & Sohyung Park, *Suicidal Death by Nicotine Poisoning*, 38 KOR.J. L. MED. 167,169 (2014).

¹² Robert A. Bassett, Kevin Osterhoudt & Tecla Brabazon, *Nicotine poisoning in an infant, 370* NEW ENG. J. MED. 2249 (2014).

¹³ J.M Cameron, D.N Howell, J.R White, D.M Andrenyak, M.E Layton & J.M Roll, Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions, 23 (1) TOBACCO CONTROL, 77 (2014).

overdosing and the severe effects that may accompany an overdose. Whereas a 175 pound adult may be able to ingest 200 mg of liquid nicotine without fatal consequences, a 40 pound child ingesting the same amount (or absorbing it through their skin) is at significantly higher risk of serious health consequences.

Perhaps more unique to the problem of e-cigarette liquid nicotine safety is the attractive presentation of e-cigarette liquid for children. Part of the growth of the e-cigarette industry has emerged from its flavored solutions, giving e-cigarette users the opportunity to select from flavors such as cotton candy, bubble gum, or a mixture of fruits.¹⁴ These flavors (and their scents) can be attractive to young children who may mistake the liquid for candy and choose to explore its taste. This possibility, in concert with the absence of protective packaging, represents a significant risk for the safety of children.¹⁵

This confluence of factors and the growth of e-cigarette use has been accompanied by an increase in nicotine poisoning episodes in the United States. The American Association of Poison Control Centers (AAPCC) maintains data on the nature of the calls to the poison control centers in the United States. In the last five years, the annual number of calls for liquid nicotine exposure has increased from 27 cases in 2011 to 3,783 cases in 2014.¹⁶ Children aged 0 to 5 make up the largest proportion of this group and are also the age group that has experienced the most dramatic increase in exposure per month.¹⁷

The lack of regulation of e-cigarettes is a key factor in the growth of liquid nicotine poisoning cases. One method to better manage the safety risk of liquid nicotine is to enact child-resistant packaging laws for the liquid nicotine products. Child resistant packaging laws have historically been successful in safe guarding children against oral ingestion of potentially poisonous substances. ¹⁸ In studies on risk and protective factors for childhood accidental poisonings, child-resistant packaging is among the leading protective measures against pediatric poisoning and has been shown to reduce nearly 40% of the number of ingestions of hazardous products by children.¹⁹

At this point, three states—Minnesota, New York, and Vermont—have fully implemented childresistant packaging laws for liquid nicotine, with at least twelve others in the process of implementation at the beginning of 2016.²⁰ Although the statistics are too small to generate any significant conclusions on the effectiveness of the laws, there have been some promising results thus far. In particular, Minnesota has experienced a 20% decrease in pediatric liquid nicotine exposures per month in 2015 after implementing the new regulations. This reduction reverses the

¹⁴ Id.

¹⁵ Bassett, *supra* note 12.

¹⁶ American Association of Poison Controls, *Electronic Cigarettes and Liquid Nicotine Data*, June 30, 2015, https://aapcc.s3.amazonaws.com/files/library/E-cig__Nicotine_Web_Data_through_7.2015_YvGFmyU.pdf. ¹⁷ Vakkalanka, *supra* note 10, at 543.

¹⁸ GB Rodgers, *The safety effects of child-resistant packaging for oral prescription drugs: two decades of experience*, 275 (21) J. AM. MED. ASS'N 1661, 1662-1663 (1996).

¹⁹ Omar. ul Hassan, Hasana Qadri, Umer Mir, & Bilal Ahmed Unintentional childhood poisoning, epidemiology and strategies for the prevention and policy change in Pakistan, 25 (3) J. AYUB MED. C. ABBOTTABAD, 90,91 (2013), http://www.ayubmed.edu.pk/JAMC/25-3/Omer.pdf.

²⁰ Tobacco Control Legal Consortium, U.S. E-Cigarette Regulations - 50 State Review (May 22, 2015) http://publichealthlawcenter.org/resources/us-e-cigarette-regulations-50-state-review.

trajectory of a 35% increase in nicotine poisonings from 2013 to 2014, prior to the implementation of child packaging laws.

A more comprehensive policy requiring child-resistant packaging for e-cigarette liquid has the potential to neutralize some of the dangers with liquid nicotine and should reduce the number of accidental poisonings among children in the United States. Even though a lack of regulatory oversight has resulted in inconsistent labeling, insufficient or nonexistent child protective packaging, and product design and flavoring that may encourage children to explore and ingest these products, and the death of at least one child,²¹ the FDA has the authority to solve this problem and prevent a public health disaster.

III. The FDA has several regulatory tools with which to solve this problem.

The broad powers of the Tobacco Control Act provide several options for the FDA to deal with the problem presented by the rise in nicotine poisoning. Each of the options has benefits and detriments but because these powers are not mutually exclusive, the agency can use all of the available tools to fully solve this problem. In considering action, the FDA should recognize that as states continue to grapple with this issue as well, maximizing the public health benefits of child-resistant packaging requires collaboration between the federal government and state and local governments. Information sharing between the levels of government will ensure that all regulators have the best information. The FDA should also consider establishing a policy that only sets a floor, allowing state and local governments to more stringently regulate packaging. Such a policy ensures that state and local governments can continue to be laboratories of democracy, experimenting with policies that the FDA may want to consider implementing at the federal level. Setting a floor rather than a ceiling also ensures that there is comprehensive protection from nicotine poisoning but still allows local communities to establish additional regulations to suit their specific needs.

a. The FDA must combat nicotine poisoning through the use of its authority to authorize the sale of new tobacco products.

The FDA's role as gatekeeper of the tobacco product market is perhaps one of the most powerful and important tools available to the agency. The FDA's authority to prevent harmful new products from ever entering the retail market represents an initial step towards finally ending the tobacco epidemic in the United States. Upon the finalization of the deeming regulation, the agency will have full premarket review authority over e-cigarettes, nicotine liquid, nicotine gel, and any other products that represent a potential poisoning danger to infants and children.

When these products are finally under FDA authority, manufacturers will have three pathways available to market new products, the Premarket Tobacco Product Application (PMTA) pathway, Substantial Equivalence (SE) report pathway, and the Exemption from Substantial Equivalence pathway. For the SE and SE Exemption pathways, a manufacturer must be able to identify a predicate product with which to compare the product yet to be marketed. The Tobacco Control Act establishes only two types of products that are eligible to be used as predicates: 1) a product that was commercially marketed, not test marketed, in the United States as of February 15, 2007,

²¹ Bassett, *supra* note 12.

called a grandfathered tobacco product, or 2) a product that has already been authorized for sale under the SE pathway.²² While at least one manufacturer has claimed to have marketed an ecigarette that could be an eligible grandfathered tobacco product,²³ this claim has not been verified and it is likely that, because of the tremendous changes of these products over time, any such product marketed in 2007 would be significantly different from currently marketed products to such a degree that a manufacturer could not establish, according to the requirements in the Act, that the predicate and a new product are substantially equivalent. Because of this likelihood, the SE and SE Exemption pathways will be unavailable for products that contain liquid nicotine. This leaves only the PMTA pathway available to manufacturers who wish to sell products that contain liquid nicotine.

The PMTA pathway is the most stringent pathway for new products, requiring the most rigorous science and most stringent review by the agency. The FDA is required to deny any application that fails a specific set of criteria, including if there is a "lack of a showing that permitting such tobacco product to be marketed would be appropriate for the protection of public health."²⁴ In establishing this criteria, Congress instructed the agency that, "the finding as to whether the marketing of a tobacco product for which an application has been submitted is appropriate for the protection of public health shall be determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product. . . ."²⁵ As is stated above, there is no question that the public health standard is intended to be broad enough to allow the FDA to protect infants and children from nicotine poisoning.

The FDA need not promulgate an additional rule in order to require child-resistant packaging through the premarket review process. The agency has broad enforcement discretion as a part of that process that can be used to protect public health in a variety of ways, including requiring child-resistant packaging.²⁶ Either as a part of the published final rule deeming all tobacco products to be within the FDA's jurisdiction or as a separate guidance to the regulated industry, the FDA should communicate that the agency, in its discretion, has determined that any product containing liquid nicotine that is proposed to be sold in a package that is not child-resistant will not be authorized for sale and the marketing of the product would not be appropriate for the protection of public health. The FDA must consider child-resistant packaging to be one of the agency's criteria in assessing a PMTA for a product containing liquid nicotine. No products that contain liquid nicotine should be authorized for sale without child-resistant packaging.

b. The FDA must establish a product standard to combat nicotine poisoning

In addition to the FDA's authority to authorize the sale of new products, the agency has specific authority to establish product standards for all regulated tobacco products. The authority to establish such a standard is broad with only a few specific limitations. The Act provides no

²² Tobacco Control Act, § 905(j)(1)(A).

²³ Altria Offers Atlantic Vapor Seven Figure Deal For Ecig Predicate Product, PRNewswire.Com, http://www.prnewswire.com/news-releases/altria-offers-atlantic-vapor-seven-figure-deal-for-ecig-predicate-product-300038991.html.

²⁴ Tobacco Control Act, § 910(c)(2)(A).

²⁵ Tobacco Control Act, § 910(c)(4).

²⁶ Eric Lindblom, *Effectively Regulating E-Cigarettes and Their Advertising – and the First Amendment*, 70 FOOD AND DRUG L. J., 57 (2015).

specific definition for the term product standard but imposes one such standard immediately, a prohibition on characterizing flavors in cigarettes with the exception of tobacco and menthol,²⁷ and also contemplates that product standards may include: 1) "provisions respecting the construction, components, ingredients, additives, constituents, including smoke constituents, and properties of the tobacco product;"²⁸ 2) "provisions for the testing (on a sample basis or, if necessary, on an individual basis) of the tobacco product;"29 3) "provisions for the measurement of the tobacco product characteristics of the tobacco product;"³⁰ 4) "provisions requiring that the results of each or of certain of the tests of the tobacco product required to be made . . . show that the tobacco product is in conformity with the portions of the standard for which the test or tests were required;"³¹ and 5) "a provision requiring that the sale and distribution of the tobacco product be restricted but only to the extent that the sale and distribution of a tobacco product may be restricted under a regulation under section 906(d)."³² The Act also specifically allows the FDA to require labeling on a product and to require that foreign grown tobacco meet the same standards as domestically grown tobacco.³³ The only specific limits on this authority prohibits the FDA from "banning all cigarettes, all smokeless tobacco products, all little cigars, all cigars other than little cigars, all pipe tobacco, or all roll-your-own tobacco products,"³⁴ and from "requiring the reduction of nicotine yields of a tobacco product to zero."³⁵

The establishment of a product standard requiring child-resistant packaging for liquid nicotine is within the agency's broad authority. It is also consistent with Congress's madate that the FDA act to protect public health. In promulgating a rule establishing a product standard, the agency is required to consider "the risks and benefits to the population as a whole, including users and nonusers of tobacco products"³⁶ Child-resistant packaging protects public health by protecting infants and children from the potential poisoning danger caused by liquid nicotine. The protection of these nonusers of tobacco products is a required consideration of the agency and establishing a product standard requiring child-resistant packaging is the best way to achieve the goal of protecting public health.

Establishing a product standard requiring child-resistant packaging also triggers important enforcement tools for the FDA to ensure that all products meet the required standard. The introduction of a tobacco product that does not meet a tobacco product standard renders such a product "adulterated,"³⁷ and if such product is required to bear specific labeling and does not, such a product is "misbranded."³⁸ The introduction of misbranded or adulterated products is prohibited under the Food Drug and Cosmetic Act,³⁹ and subject to civil penalties of \$15,000 for

²⁷ Tobacco Control Act, § 907(a)(1).

²⁸ Tobacco Control Act, § 907(a)(4)(B)(i).

²⁹ Tobacco Control Act, § 907(a)(4)(B)(ii).

³⁰ Tobacco Control Act, § 907(a)(4)(B)(iii).

³¹ Tobacco Control Act, § 907(a)(4)(B)(iv).

³² Tobacco Control Act, § 907(a)(4)(B)(v).

³³ Tobacco Control Act, § 907(a)(4)(C) & (D).

³⁴ Tobacco Control Act, § 907(d)(3)(A).

³⁵ Tobacco Control Act, § 907(d)(3)(B).

³⁶ Tobacco Control Act, § 907(a)(3)(B)(i)(I).

³⁷ Tobacco Control Act, § 902(5).

³⁸ Tobacco Control Act, § 903(a)(9).

³⁹ 21 U.S.C. § 331(a).

each violation,⁴⁰ or \$250,000 if the violation is intentional.⁴¹ In addition, misbranded or adulterated products are subject to seizure by the agency at any time.⁴² All of these penalties can be imposed on any entity that is a part of the supply chain: manufacturers, importers, wholesalers, distributors, and retailers. The FDA's powers to enforce product standards are broad and robust.

In the development of a product standard requiring child-resistant packaging, it would be wise for the FDA's Center for Tobacco Products to work closely with the Consumer Product Safety Commission as that agency has significant expertise in regulating child-resistant packaging. Congress has also instructed the FDA to consult with other agencies as it develops product standards;⁴³ consultations with the CPSC and other FDA centers that have experience with child-resistant packaging would fulfill this directive and would maximize the effectiveness of a final rule requiring child-resistant packaging.

As is stated above, the FDA must waste no time in implementing a policy requiring childresistant packaging. By default, the Act requires that a product standard take effect one year after a final rule is published. However, if the Secretary determines that "an earlier effective date is necessary for the protection of the public health,"⁴⁴ the effective date can be moved up. In developing a product standard for child-resistant packaging, the FDA should implement a rule as early as is feasible for the regulated industry. Because many states are already establishing requirements, there is already a market for compliant packaging and thus, this rule could likely be implemented in as little as 30-60 days.

It must also be stated that while the expertise of the Tobacco Product Scientific Advisory Committee is indispensable to the agency and the committee's value is unquestionable, the issue of nicotine poisoning is not complicated enough to warrant investigation and recommendation by the committee. This is a straightforward problem with a relatively simple solution. Referral of a potential product standard to TPSAC is discretionary rather than mandatory,⁴⁵ and in this case would add unnecessary delay to the FDA's process. We urge the agency to act quickly on childresistant packaging.

c. The FDA should adopt a policy that is comprehensive in nature and grants no exemptions for any products.

The FDA should be aware that as states have begun pursuing policy options for implementing child-resistant packaging, many have seen opposition from product manufacturers and/or industry lobbyist pushing for exemptions for certain products. There has been a particularly fervent push to exempt products that include nicotine where a consumer is not intended to access the nicotine. However, if these products truly feature nicotine that is in accessible in a form that can be ingested, they would likely comply with child-resistant packaging requirements. Therefore, any exemption based on the accessibility or inaccessibility of the nicotine is

⁴⁰ 21 U.S.C. § 333(f)(9)(A).

⁴¹ 21 U.S.C. § 333(f)(9)(B).

⁴² 21 U.S.C. § 334.

⁴³ Tobacco Control Act, § 907(a)(6)(B).

⁴⁴ Tobacco Control Act, § 907(d)(2).

⁴⁵ Tobacco Control Act, § 907(d)(5).

unwarranted, unnecessary, and could potentially have unforeseen consequences that harm public health. The FDA should ensure that its requirements for child-resistant packaging are comprehensive in scope.

In the agency's request for comments, the FDA has specifically asked if it should establish childresistant packaging requirements for other novel tobacco products such as dissolvables, lotions, gels, and drinks. We strongly urge the FDA to ensure that any product that contains nicotine in a form that can be easily ingested or absorbed transdermally only be sold in child-resistant packaging. As long as there is a possibility for infants and children to access dangerous or even deadly quantities of nicotine, the FDA should require that such a product be sold in childresistant packaging. There is no reason to exempt such products and to do so would significantly reduce the potential benefits of a rule requiring child-resistant packaging.

IV. The FDA must protect public health by requiring child-resistant packaging for all products that contain nicotine in a form that is easily ingestible.

The rise in popularity of e-cigarettes has led to a corresponding increase in the prevalence of nicotine poisoning. The FDA is the agency best suited to comprehensively address this problem throughout the country. In order to provide the maximum benefit to public health, the FDA must require child-resistant packaging for all products that contain nicotine in an easily ingestible or absorbable form regardless of any attributes of a product.

Respectfully,

Association of Maternal & Child Health Programs Association of State and Territorial Health Officials ClearWay Minnesota Minnesota Poison Control System Safe Kids California Safe Kids Kansas Tobacco Control Legal Consortium Tobacco Control Network Truth Initiative