

# How Might Manufacturers of E-Cigarettes Get New Product and MRTP Orders from FDA More Quickly and Easily?

ERIC N. LINDBLOM\*

## ABSTRACT

According to manufacturers and some members of the public health and tobacco control communities, exclusively using e-cigarettes is much less harmful and risky to users and exposed nonusers than tobacco smoking. But federal law prohibits manufacturers and importers from labeling or marketing their e-cigarettes as delivering fewer toxins or being less harmful than cigarettes or other smoked tobacco products unless they first obtain permissive orders from FDA. Being allowed to make such reduced-exposure or reduced-risk claims would help a manufacturer attract smokers to use its e-cigarettes instead, giving them a powerful new competitive advantage. But no e-cigarette company has yet applied to FDA to obtain the new product and modified risk tobacco product (MRTP) orders they need to be allowed to market their e-cigarettes as less toxic or less harmful to use. Apparently, the process for obtaining the necessary permissive orders from FDA is too complicated, costly, and uncertain even to be worth trying. This paper suggests a way that e-cigarette companies might secure new product and MRTP orders more quickly and easily—or at least establish a test case that could prompt the courts to ensure that the order process provides a reasonable way for e-cigarettes to enter or stay on the U.S. market and be advertised with reduced-risk claims, consistently with FDA’s statutory duty to protect the public health.<sup>1</sup>

## INTRODUCTION

E-cigarettes are uniquely positioned to serve as less-harmful alternatives to smoking because they enable users to inhale nicotine into their lungs, as smokers do, but without using any combustion or tobacco. By delivering nicotine from a liquid solution in aerosol form without combustion, e-cigarettes can sharply reduce user and nonuser

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\* Eric N. Lindblom is the Director for Tobacco Control and Food & Drug Law at Georgetown Law’s O’Neill Institute for National & Global Health Law, and the former Director of the Office of Policy at FDA’s Center for Tobacco Products (2011-2014). Before FDA, Mr. Lindblom was General Counsel and Director for Policy Research at the Campaign for Tobacco-Free Kids.

<sup>1</sup> This paper grew out of a discussion at the FDLI Annual Conference’s Risk-Based Regulation of Tobacco Products breakout session, May 4, 2018. Although the proposed strategy focuses on e-cigarettes (loosely defined as any product that delivers nicotine into the lungs of consumers without either tobacco or combustion), it might also be used by companies selling certain smokeless tobacco products or other non-smoked tobacco-nicotine products that research has established or indicates are less harmful to consume than smoked tobacco products.

exposure to many carcinogens and other harmful or potentially harmful constituents.<sup>2</sup> Although there is considerable uncertainty and controversy about the relative harmfulness of exclusively using e-cigarettes compared to tobacco smoking,<sup>3</sup> some research reviews have concluded that they are or are likely considerably less harmful than cigarettes or smoking.<sup>4</sup> Manufacturers and others in the tobacco industry typically refer to e-cigarettes as reduced-harm products,<sup>5</sup> and some members of the public health and tobacco control communities support stronger measures to shift smokers to e-cigarettes to reduce overall tobacco-related harms.<sup>6</sup>

Under current law, however, manufacturers and importers of e-cigarettes may not label or advertise them as delivering fewer toxins or as being less-harmful than tobacco smoking without first obtaining a permissive modified risk tobacco product (MRTP) orders from FDA, which also requires having a new product order allowing the e-cigarette to enter or stay on the market.<sup>7</sup> To issue such an order, FDA must determine

<sup>2</sup> See, e.g., Jeffrey Drope et al., *Key Issues Surround the Health Impacts of Electronic Nicotine Delivery Systems (ENDS) and Other Sources of Nicotine*, 67 CA 449 (2017).

<sup>3</sup> See, e.g., NAT'L ACADS. SCIS. ENGINEERING & MED., PUBLIC HEALTH CONSEQUENCES OF E-CIGARETTES 1–8, 33 (Kathleen Stratton et al. eds., 2018) (concluding that “[t]o the extent that laboratory tests of e-cigarette ingredients, in vitro toxicological tests, and short-term human studies suggest that e-cigarettes are likely less harmful than combustible tobacco cigarettes, due to lack of long-term epidemiological studies and large clinical trials, the implications for long-term effects on morbidity and mortality are not yet clear and the absolute safety of the products cannot be unambiguously assessed at this time . . .”). For examples of the ongoing dispute over the relative harmfulness of exclusive e-cigarette use versus smoking, see Boris Reidel et al., *E-Cigarette Use Causes a Unique Innate Immune Response in the Lung Involving Increased Neutrophilic Activation and Altered Mucin Secretion*, 197 AM. J. RESPIRATORY & CRITICAL CARE MED. 492, 1 (2018) (“our results challenge the concept that e-cigarettes are a healthier alternative to cigarettes and reverse smoking-induced adverse health effects”); Editorial, *E-Cigarettes: Public Health England’s Evidence-Based Confusion*, 386 LANCET 829 (2015); Ann McNeill et al., *E-Cigarettes: The Need for Clear Communication on Relative Risks*, 386 LANCET 1237, 1237 (2015); David J. Nutt et al., *E-Cigarettes are Less Harmful Than Smoking*, 387 LANCET 1160 (2016); Martin McKee & Simon Capewell, *Electronic Cigarettes: We Need Evidence, Not Opinions*, 386 LANCET 1239 (2015).

<sup>4</sup> See, e.g., ANN MCNEILL ET AL., EVIDENCE REVIEW OF E-CIGARETTES AND HEATED TOBACCO PRODUCTS 2018: A REPORT COMMISSIONED BY PUBLIC HEALTH ENGLAND 20 (2018), <https://www.gov.uk/government/publications/e-cigarettes-and-heated-tobacco-products-evidence-review> (“Based on current knowledge, stating that vaping is at least 95% less harmful than smoking remains a good way to communicate the large difference in relative risk unambiguously . . .”); Drope, *supra* note 2 at 451 (“The preponderance of the scientific evidence to date suggests, however, that current-generation ENDS products are demonstrably less harmful than combustible tobacco products, such as conventional cigarettes, in several key ways.”).

<sup>5</sup> See, e.g., *Harm Reduction At-A-Glance*, ALTRIA, <http://www.altria.com/Responsibility/Tobacco-Harm-Reduction/Pages/default.aspx> (last accessed Nov. 16, 2018); *Tobacco Harm Reduction*, REYNOLDS AM., <http://sustainability.reynoldsamerican.com/tobacco-harm-reduction> (last accessed Nov. 16, 2018).

<sup>6</sup> See generally, e.g., Kenneth E. Warner, *How to Think—Not Feel—About Tobacco Harm Reduction*, NICOTINE & TOBACCO RES. (April 30, 2018) <https://academic.oup.com/ntr/advance-article/doi/10.1093/ntr/nty084/4990310>; Lynn T. Kozlowski & David B. Abrams, *Obsolete Tobacco Control Themes can be Hazardous to Public Health: The Need for Updating Views on Absolute Product Risks and Harm Reduction*, 16 BMC PUB. HEALTH 432 (2016); Clive Bates, *53 Public Health Specialists Write to WHO About Alternatives to Smoking—Here’s the Letter*, COUNTERFACTUAL BLOG (May 29, 2014) <https://www.clivebates.com/53-public-health-specialists-writeto-who-about-alternatives-to-smoking-heres-the-letter> [<https://perma.cc/UN95-L8BH>].

<sup>7</sup> Family Smoking Prevention and Tobacco Control Act, H.R. 1256, 111th Cong. §§ 911, 910, 21 U.S.C. § 387k, j (2009) [hereinafter TCA]; See, also, FOOD & DRUG ADMIN., GUIDANCE: EXTENSION OF CERTAIN TOBACCO PRODUCT COMPLIANCE DEADLINES RELATED TO THE FINAL DEEMING RULE (REVISED) (2017).

that allowing the MRTP claim would be beneficial for the public health.<sup>8</sup> Being able to make such attractive claims, when other e-cigarette companies may not, would give an e-cigarette seller an enormous competitive advantage and boost its sales. Yet, no e-cigarette manufacturer has applied to FDA for permission to do so.<sup>9</sup> It is likely that manufacturers see the application process as overly complicated, difficult, and expensive—perhaps prohibitively so for smaller companies—with only limited chances of success. Indeed, the viable applications filed by other tobacco products for new product and MRTP orders have typically consisted of tens of thousands of pages and extensive revisions and supplementary submissions.<sup>10</sup> But FDA has rejected hundreds of new product applications and issued only a handful of permissive new product orders, and FDA has issued no MRTP orders to date.<sup>11</sup>

This paper suggests a new, quicker, simpler strategy that e-cigarette companies could follow to try to obtain the new-product and MRTP orders they need from FDA to put or keep their products on the U.S. market legally and to market them with reduced-risk claims. Even if unsuccessful, following the proposed approach and getting an FDA rejection would still establish a test case that could be used to try to prompt the courts to direct FDA to establish a more reasonable and effective process for seeking and obtaining new product and MRTP orders. E-cigarette companies could adopt this proposed strategy purely for profit-seeking business reasons. But this approach could also benefit the public health if it paved the way for more rapid technological development to replace more-harmful e-cigarettes currently on the market with less-harmful versions, or if it enabled companies to make accurate relative-risk claims that encouraged smokers who would not otherwise quit to switch to truly less-harmful e-cigarettes (without also producing offsetting health-harming impacts).

As detailed below, the basic strategy consists of submitting a good-faith application for a new-product and MRTP order directed specifically at producing significant net public health gains while minimizing the risks of any health-harming impacts. Put simply, the applicant would bend over backward to structure the applicant e-cigarette and its proposed marketing to minimize the risks of creating any new public health harms, while still providing for at least some net public health gains. The product and its marketing, as proposed in the application, would focus as directly as possible only on encouraging smokers who would not otherwise quit to switch completely to using the e-cigarettes. At the same time, the proposed product and marketing would be designed, to the extent possible, to reduce the risk of creating any health-harming impacts, such as preventing or delaying smoking or total cessation, increasing relapse among former smokers who would not otherwise relapse, prompting initiation among

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<sup>8</sup> TCA, *supra* note 7, at § 911(g), 21 U.S.C. § 387k(g).

<sup>9</sup> *Modified Risk Tobacco Products: MRTP Applications Currently Under Scientific Review*, FOOD & DRUG ADMIN., [www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm304465.htm#2](http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm304465.htm#2) (last accessed Nov. 16, 2018) [hereinafter *Modified Risk*].

<sup>10</sup> *Modified Risk* *supra* note 9; *Tobacco Product Marketing Orders*, FOOD & DRUG ADMIN., [www.fda.gov/tobaccoproducts/labeling/tobaccoproductreviewevaluation/ucm339928.htm](http://www.fda.gov/tobaccoproducts/labeling/tobaccoproductreviewevaluation/ucm339928.htm) (last accessed Nov. 16, 2018) [hereinafter *Tobacco Product Marketing Orders*]; *See also, Premarket Tobacco Applications*, FOOD & DRUG ADMIN., <https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/PremarketTobaccoApplications/ucm304506.htm> (last accessed Nov. 16, 2018). *See also, infra* notes 23 and 24.

<sup>11</sup> *Modified Risk* *supra* note 9; *Tobacco Product Marketing Orders*, *supra* note 10.

youth or adults who would not otherwise use any tobacco-nicotine product, or increasing dual use that does not accelerate cessation. That done, the applicant would request a prompt decision from FDA based on the application as submitted, and then go to court for relief if FDA did not issue a permissive order within a reasonable period of time.<sup>12</sup>

## THE CURRENT SITUATION

Companies that want to market e-cigarettes as less-harmful alternatives to smoked tobacco products face several regulatory challenges. Pursuant to the FDA rule deeming all tobacco products (including non-drug nicotine-delivery products) under its tobacco control jurisdiction and FDA's related guidance, manufacturers or importers of e-cigarettes already sold in the U.S. when the deeming rule went into effect must, to stay on the market, submit an application by August 8, 2022 to obtain a new-product order,<sup>13</sup> and FDA must subsequently find that the applicant has shown that it would be "appropriate for the protection of the public health" to allow the e-cigarettes to continue being sold.<sup>14</sup> The companies could instead seek to obtain an order allowing the e-cigarettes to stay on the market just by showing that their e-cigarettes are "substantially equivalent" to an e-cigarette that was on the market as of February 15, 2007.<sup>15</sup> But it is unlikely that e-cigarettes currently on the U.S. market could be found substantially equivalent to any early models that might have been on the U.S. market more than eleven years ago.

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<sup>12</sup> Whether such legal action might be necessary is uncertain. It is possible that FDA would issue permissive orders in response to applications that followed the approach proposed here, and would not take too long to do so. Although FDA is currently taking a considerable amount of time to evaluate new product and MRTP applications, that could be caused primarily by the applicants submitting voluminous applications that require enormous amounts of time to review and evaluate carefully and then continually amending them. Moreover, none of the new product or MRTP applications filed to date have simplified the process and increased their chances of getting a permissive order by proposing to target the delivery of their advertising or their reduced-risk messaging to reach directly only those who could reduce their health harms and risks by using the product.

<sup>13</sup> FOOD & DRUG ADMIN., GUIDANCE: EXTENSION OF CERTAIN TOBACCO PRODUCT COMPLIANCE DEADLINES RELATED TO THE FINAL DEEMING RULE (REVISED) (2017). These applications are referred to as Premarket Tobacco Applications or PMTAs. Pursuant to the clear terms of the TCA, all e-cigarettes on the U.S. market after FDA's implantation of the final deeming rule are on the market illegally and must obtain a substantial equivalence or new product order to be allowed on the market legally. TCA, *supra* note 7, at §§ 905(j); 910(a), 21 U.S.C. § 387e(j), j(a). In its deeming rule and the Guidance cited above, FDA has announced that it will exercise its enforcement discretion and not enforce against any e-cigarettes now illegally on the market that were legally on the market immediately prior to the deeming effective date, so long as they submit a new product order by August 8, 2022. Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products (Deeming Rule), 81 Fed. Reg. (2016) [21 C.F.R. §§ 1100, 1140, 1143].

<sup>14</sup> TCA, *supra* note 7, at § 910, 21 U.S.C. § 387j. Allowing a new tobacco product on the market would be "appropriate for the protection of the public health" if its availability, marketing, and sale (subject to any requirements and restrictions in the order) would produce a net benefit to the health of the population as a whole, taking in consideration the impacts not only on users but on nonusers, including impacts on cessation, relapse, initiation, dual use, etc. A big public health gain is not required, just some non-trivial net gain to the health of the population as a whole.

<sup>15</sup> TCA, *supra* note 7, § 905(j), 21 U.S.C. § 387e(j).

E-cigarettes not yet on the U.S. market must also obtain a permissive new product order from FDA before they can be legally sold.<sup>16</sup> Similarly, any company that wants to make any significant technological improvements or other substantial changes to an e-cigarette already on the market (including changes to make it less harmful) must also first secure a permissive new-product order.<sup>17</sup> Here, too, FDA may allow the substantially changed or brand-new e-cigarette onto the U.S. market only if it finds that the company's application has established that it would be "appropriate for the protection of the public health" for FDA to do so.<sup>18</sup>

If the company also wants to market its e-cigarettes as a less-harmful alternative to smoking—and make related reduced-risk or reduced-exposure claims on the product's labeling or in its advertising—the manufacturer must first apply to FDA to obtain a permissive MRTP order.<sup>19</sup> To get the order, the applicant company must convince FDA that the product and its marketing with the claim will not only "significantly reduce harm and the risk of tobacco-related disease to individual tobacco users," but will also "benefit the health of the population as a whole."<sup>20</sup>

Although product development and technological improvements have, presumably, continued since the FDA deeming rule went into effect, no e-cigarette company has yet applied for a new-product order to allow a new or improved e-cigarette onto the U.S. market.<sup>21</sup> In addition, despite the enormous competitive advantages an e-cigarette company would enjoy if it were able to make reduced-risk claims, no e-cigarette company has yet applied for an MRTP order.<sup>22</sup>

The main reason for the dearth of applications appears to be a common perception that the application process for obtaining new-product or MRTP orders is complex, expensive, and time consuming, with quite limited chances of success, especially for e-cigarette companies with limited resources. Indeed, the application by tobacco giant Philip Morris International to try to obtain new-product and MRTP orders for its heat-not-burn IQOS tobacco product has been pending since 2016, with numerous amended and supplementary submissions, and numerous responses to FDA questions and requests for clarification or additional information. The application totals in the millions of pages, with the amended Executive Summary, alone, over 200 pages long—and the public comment period does not yet have a closing date.<sup>23</sup> Swedish Match applied for an MRTP order for some smokeless "snus" products in August, 2014, and two years later received a formal response from FDA denying part of its application and deferring the rest (subject to Swedish Match conducting new studies, compiling additional evidence, and submitting a revised application). There, too, the

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<sup>16</sup> *Id.* at § 910(a)(1)(A) [21 U.S.C. § 387j(a)(1)(A)]

<sup>17</sup> *Id.* at § 910(a)(1)(B) [21 U.S.C. § 387j(a)(1)(B)].

<sup>18</sup> *Id.* at § 910(c)(2)(A), (c)(4) [21 U.S.C. § 387j(c)(2)(A), j(c)(4)].

<sup>19</sup> *Id.* at § 911 [21 U.S.C. § 387k].

<sup>20</sup> *Id.* at § 911(g)(1) [21 U.S.C. § 387k(g)(1)]. This standard directly parallels the "appropriate for the protection of the public health" standard. *Supra*, note 18.

<sup>21</sup> *Tobacco Product Marketing Orders*, *supra* note 10.

<sup>22</sup> *Modified Risk*, *supra* note 9.

<sup>23</sup> *Philip Morris Products S.A. Modified Risk Tobacco Product (MRTP) Applications*, FOOD & DRUG ADMIN., [www.fda.gov/tobaccoproducts/labeling/marketingandadvertising/ucm546281.htm](http://www.fda.gov/tobaccoproducts/labeling/marketingandadvertising/ucm546281.htm) (last accessed Nov. 16, 2018).

application consisted of hundreds of thousands of pages, including numerous amended and supplementary filings.<sup>24</sup>

Although some might see this situation as a problem solely for profit-seeking companies seeking to maximize their sales of e-cigarettes or other tobacco-nicotine products, such high entry barriers could also have significant public health consequences. Preventing or delaying e-cigarettes or other tobacco-nicotine products from getting onto the market that are less harmful than those currently being sold or significantly more attractive as smoking substitutes could prevent or delay related public health gains. Preventing or delaying manufacturers from marketing truly less-harmful e-cigarettes or other non-combusted tobacco-nicotine products to smokers as less-harmful alternatives could also dampen switching by smokers who will otherwise continue smoking.

### **NEW STRATEGY FOR OBTAINING FDA NEW-PRODUCT AND MRTP ORDERS FOR E-CIGARETTES**

This step-by-step strategy is relatively simple. It proposes a way that applicants could possibly obtain new-product and MRTP orders promptly from FDA without submitting thousands of pages of application documents and supporting materials, and without months of back and forth responding to FDA questions and requests. It calls for the applicant company to offer a reliable, well-designed, and properly manufactured e-cigarette, and to do everything it can to structure its application and the subject e-cigarette to make allowing it on the market with a reduced-risk claims as clearly “appropriate for the protection of the public health” as possible.<sup>25</sup>

The goal is not to show FDA how large the maximum potential health gains might be, but to assure FDA that allowing the e-cigarette on the market with reduced-risk claims (as proposed in the application) would, at worst, produce little or no risk of creating any net negative impact on the public health of any significance, and would be much more likely to produce a net health benefit. To promote that goal, the company submitting the application would take all available steps to maximize the risk reductions from using the applicant e-cigarette instead of smoking, focus its proposed marketing and reduced-risk claims only at smokers, notify smokers of the extra risks from dual use and the extra health gains from quitting all use, and limit the extent to which allowing the e-cigarette’s marketing or reduced-risk claims might produce any health-harming impacts (or raise any related concerns among those reviewing the application).<sup>26</sup>

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<sup>24</sup> *Swedish Match North America, Inc., MRTP Applications*, FOOD & DRUG ADMIN., [www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm533454.htm](http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm533454.htm) (last accessed Nov. 16, 2018). R.J. Reynolds has also submitted an application to obtain an MRTP order for certain smokeless snus products, which also already consists of many thousands of pages. *R.J. Reynolds Tobacco Company Modified Risk Tobacco Product (MRTP) Applications*, FOOD & DRUG ADMIN., [www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm564399.htm](http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm564399.htm) (last accessed Nov. 16, 2018).

<sup>25</sup> TCA, *supra* note 7, § 910(c)(2)(a) & § 911(g)(1)(B) [21 U.S.C. § 387j(c)(2)(a) and § 387k(g)(1)(B)].

<sup>26</sup> On the possible extra health harms and risks from dual use (smoking and using e-cigarettes) compared to just smoking, see, e.g., Talal Alzahrani et al., *Association Between Electronic Cigarette Use and Myocardial Infarction*, 55 AM. J. PREVENTIVE MED. 455 (2018); Vladimir B. Vladimir B. Mikheev et al., *Real-Time Measurement of Electronic Cigarette Aerosol Size Distribution and Metals Content Analysis*, 18 NICOTINE & TOBACCO RES. 1895 (2016). *But see*, Hayden McRobbie et al., *Effects of Switching to*

Here's how that might be done:

(1) *Eliminate any features of the e-cigarette that might raise avoidable public health concerns.* At the very least, this entails minimizing contamination and eliminating any potentially toxic or harmful ingredients that are not necessary to the e-cigarette's operation, such as flavorings or other additives that are harmful or potentially harmful constituents (HPHCs) or that create HPHCs when consumed in the e-cigarette.<sup>27</sup> Ideally, nicotine would be the only HPHC in the product.

To make the application even stronger, the subject e-cigarette would also forgo any added non-HPHC flavors that are or might be seen as especially attractive to youth. For the strongest case, the only proposed added flavors might be tobacco or menthol, which could be defended as necessary for attracting smokers of regular and menthol cigarettes (the only flavors allowed for cigarettes).<sup>28</sup> Ideally, the only additional flavors the applicant e-cigarette would propose would be those that reputable published research finds, or at least indicates, would do much more to increase sustained smoker switching than increase initiation by youth who would not otherwise smoke or use tobacco-nicotine products.<sup>29</sup> A weaker but possibly viable option might be to include a small collection of straightforward additional non-HPHC flavors that would provide adults with some variety but did not have kid-attracting names and were not associated with products especially popular with youth (e.g., no “gummy bear”)<sup>30</sup>—along with a pledge to eliminate any of those additional flavors if research of sales data showed that these flavors were attracting youth more than adult smokers. Going further, the application could state that most or all of the flavored versions would be sold only in adult-only stores, if FDA has not already established such a sales restriction.<sup>31</sup>

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*Electronic Cigarettes with and without Concurrent Smoking on Exposure to Nicotine, Carbon Monoxide, and Acrolein*, 8 CANCER PREVENTION RES. 873 (2015).

<sup>27</sup> The reference to HPHCs here is meant to include any harmful or potentially harmful constituents, not just those on any existing FDA or other lists of HPHCs. *See, e.g.*, Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke: Established List, 77 Fed. Reg. (Apr. 3, 2012).

<sup>28</sup> *See, e.g.*, Mark D. Litt et al., *Cigarette Smoking and Electronic Cigarette Vaping Patterns as a Function of E-Cigarette Flavourings*, 2 TOBACCO CONTROL SUPPL. ii67 (2016).

<sup>29</sup> *See, e.g.*, Meghan E. Morean et al., *Preferring More E-Cigarette Flavors is Associated with E-Cigarette Use Frequency Among Adolescents but Not Adults*, 13 PLOS ONE 1 (2018). An applicant could also point out that going beyond avoiding clearly kid-attracting flavors and flavor names to prohibit or severely limit the applicant e-cigarette's use of any non-HPHC flavors would do little to protect against non-smoker youth initiation and other undesirable impacts given the vast array of flavors existing e-cigarettes already offer and advertise—especially as any advertising of any permitted flavors for the applicant e-cigarette would be subject to the advertising restrictions described in point (4), below, which would minimize youth exposure. *See, e.g.*, Greta Hsu et al., *Evolution of Electronic Cigarette Brands from 2013-2014 to 2016-2017: Analysis of Brand Websites*, 20 J. MED. INTERNET RES. 3 e80, at 4 (2018) (finding more than 7,000 currently offered e-cigarette flavors).

<sup>30</sup> *See, e.g.*, M.B. Harrell et al., *Flavored E-Cigarette Use: Characterizing Youth, Young Adult, and Adult Users*, 55 PREVENTIVE MED. REP. 33 (2017).

<sup>31</sup> What might or might not be viable or most effective in regard to flavors for getting permissive new product and MRTP orders will depend largely on whether FDA has taken any new enforcement or rulemaking actions relating to e-cigarette flavors. As this article goes to press, FDA has promised to take

Some argue that e-cigarettes need to have many flavors other than tobacco or menthol to attract and retain switching smokers.<sup>32</sup> But existing research shows that smoker desires to quit smoking and reduce health harms and risks are more powerful factors for attracting smokers to e-cigarettes.<sup>33</sup> Accordingly, restricting flavors to make it quicker and easier to obtain an MRTP order allowing an e-cigarette to be marketed with reduced-risk claims could be beneficial from both a business and public health perspective.

(2) *Using available research and other evidence, make as strong an argument as possible that the use of the applicant e-cigarette is considerably less harmful than using some e-cigarettes currently on the market and not significantly more harmful than using any other e-cigarettes on the market.* If the applicant e-cigarette were more harmful than any e-cigarette already on the market, allowing its sale or related reduced-risk claims would not be “appropriate for the protection of the public health”<sup>34</sup> because users of less-harmful e-cigarettes might switch to the applicant product, and smokers switching to the applicant e-cigarette would be better off switching to the other available, less harmful e-cigarettes instead.<sup>35</sup> In most cases, no new research would be needed to establish that the applicant e-cigarette is less harmful than some e-cigarettes on the market and no-more harmful than others. It would likely be sufficient to show that it is a reliable, high-quality e-cigarette and, unlike many e-cigarettes already on the market, has minimal contamination and does not contain any harmful or potentially harmful ingredients other than those necessary for its operation.<sup>36</sup>

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enforcement action to restrict most flavored e-cigarette sales to adult-only stores and possibly implement a rule to ban certain e-cigarette flavors. But what, exactly, FDA will actually do, and when it will do it, is still not clear. See, e.g., FDA Statement, *Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes*, <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625884.htm> (last accessed Nov. 16, 2018); FDA Statement, *Statement from FDA Commissioner Scott Gottlieb, M.D., on new steps to address epidemic of youth e-cigarette use*, <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620185.htm> (last accessed Nov. 16, 2018).

<sup>32</sup> See, e.g., Carrie Wade, *California Needs to Think Twice About Banning Flavored E-Cigarettes*, THE HILL (June 1, 2017), <https://thehill.com/blogs/pundits-blog/state-local-politics/335976-california-needs-to-think-twice-about-banning>.

<sup>33</sup> See, e.g., Sebastian Bauhoff et al., *Perceptions of E-Cigarettes: A Comparison of Adult Smokers and Non-Smokers in a Mechanical Turk Sample*, 43 AM. J. DRUG & ALCOHOL ABUSE 311 (2017). See generally CTR. FOR SUBSTANCE USE RESEARCH, *ELECTRONIC VAPING PRODUCTS: RECOMMENDATIONS FOR A REGULATORY FRAMEWORK THAT RECOGNIZES THE POTENTIAL FOR POSITIVE HEALTH IMPACTS* (2017).

<sup>34</sup> TCA, *supra* note 7, § 910(c)(2)(a) [21 U.S.C. § 387j(c)(2)(a)].

<sup>35</sup> As noted in a recent study supported by FDA’s Center for Tobacco Products, with a CTP staff person as primary author, “since the FDA is responsible for premarket approval of new tobacco products, including e-cigarettes, over time the market would come to be dominated by the least harmful of these products.” Apalberg, B, et al., “Potential Public Health Effects of Reducing Nicotine Levels in Cigarettes in the United States,” 378 NEW ENGLAND JNL OF MEDICINE 1725 (May 2018).

<sup>36</sup> See, e.g., Rachel Z. Behar, *Comparing the Cytotoxicity of Electronic Cigarette Fluids, Aerosols and Solvents*, TOBACCO CONTROL (Apr. 10, 2018), <http://tobaccocontrol.bmj.com/content/early/2018/04/10/tobaccocontrol-2016-053472>. Diana Crow, *Some E-Cigarette Flavors May Be More Harmful*



(3) *Using available research and evidence, make as strong an argument as possible that the use of the applicant e-cigarette as a complete substitute for smoking is highly likely to be significantly less-harmful to users and exposed non-users.* Even if viewed cautiously, available published research should enable an applicant to provide a strong case, first, that exclusively using e-cigarettes is, in general, likely to be significantly less harmful to users and exposed nonusers than smoking—perhaps in roughly ten pages with citations to publicly available sources.<sup>37</sup> The applicant would then use another few pages to explain that its subject e-cigarette is even less harmful than many currently on the market (e.g., because it presents no significant explosion, fire, or burning risk; has minimal contamination; and does not contain any HPHCs other than those necessary for its operation). If the e-cigarette also has some other new design or technology that makes it even less harmful than most or all e-cigarettes already on the market, so much the better. No time or money need be spent trying to develop additional new evidence about exactly how much less harmful the specific e-cigarette might be. It would be enough to show that exclusively using e-cigarettes is generally less harmful than smoking and that the applicant e-cigarette is no more harmful than any other e-cigarettes on the market and significantly less harmful than many or most. But the summary of available research on relative harmfulness would need to be thorough, unbiased, and convincing (and avoid relying on only the most supportive research or only on those research reviews that find the largest differences in relative risk).<sup>38</sup> As a final point, the application could point out that even if exclusively using the subject e-cigarettes turned out to be just as harmful as smoking, smokers who switched would not experience any increase in harms and research indicates that exposed nonusers would still have their risks and harms reduced.<sup>39</sup>

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*Than Others*, ATLANTIC MONTHLY (Nov. 28, 2017) (referencing Allyson E. Kennedy et al., *E-Cigarette Aerosol Exposure Can Cause Craniofacial Defects in Xenopus Laevis Embryos and Mammalian Neural Crest Cells*, 12 PLOS ONE (Sept. 28, 2017)).

<sup>37</sup> See, e.g., NAT'L ACADS. SCIS. ENGINEERING & MED., *supra* note 3, at 1 (“Laboratory tests of e-cigarette ingredients, in vitro toxicological tests, and short-term human studies suggest that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes.”).

<sup>38</sup> For example, the National Academies report also found that “due to lack of long-term epidemiological studies and large clinical trials, the implications for long-term effects on morbidity and mortality are not yet clear and the absolute safety of the products cannot be unambiguously assessed at this time.” *Id.* at 33. Accordingly, an applicant would need to explain why it would still be “appropriate for the protection of the public health” for FDA to grant the related new product and MRTP orders before such long-term studies and large clinical trials could be completed. Besides referencing what the already available studies indicate, the applicant could point out that, even without such long-term research, it is clear that the subject e-cigarettes are significantly less harmful than many other e-cigarettes (e.g. no HPHC additives, less contamination). Moreover, given the sharply increased premature death risks and other enormous harms caused by smoking, even if using the subject e-cigarette were only five percent less harmful, the health benefits from complete switching or from initiating into using the e-cigarette instead of smoking would be quite significant.

<sup>39</sup> Even if secondhand e-cigarette aerosol-vapor were as harmful to exposed nonusers as secondhand tobacco smoke, e-cigarette use produces less exposure among nearby non-users. See, e.g., Dainius Martuzevicius et al., *Characterization of the Spatial and Temporal Dispersion Differences Between Exhaled E-Cigarette Mist and Cigarette Smoke*, 00 NICOTINE & TOBACCO RES. 1 (2018); Pasquale Avino et al.,

(4) Agree in the application to present the e-cigarette only as a smoking alternative and to advertise and market the e-cigarette only to adult smokers or former smokers now using e-cigarettes, while minimizing the risk of reaching youth or those not currently smoking or using e-cigarettes. This could be done by the applicant proposing that the e-cigarette be labeled for use only as an alternative to smoking, with its advertising restricted only to: (a) direct communications to pre-verified adults who self-identify as current smokers or as former smokers now using e-cigarettes (e.g., via direct mail, email, social media); (b) advertising at adult-only tobacco product retailers and vape shops; and (c) providing brochures or other advertising materials to pre-verified adults who self-verify as smokers or as former-smoker e-cigarette users at any retail sales outlets for the e-cigarette that allow youth.<sup>40</sup> These measures would ensure that the e-cigarette would be marketed directly only to those most likely to benefit (or not be harmed) from using it. It would also sharply reduce the risk that the marketing of the e-cigarette would increase initiation among otherwise non-users of tobacco-nicotine products or increase relapse among former smokers who would not otherwise relapse.<sup>41</sup>

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*Second-Hand Aerosol from Tobacco and Electronic Cigarettes: Evaluation of the Smoker Emission Rates and Doses and Lung Cancer Risk of Passive Smokers and Vapers*, 642 SCI. TOTAL ENV'T. 137 (2018). See also, Esteve Fernández, *Particulate Matter from Electronic Cigarettes and Conventional Cigarettes: A Systematic Review and Observational Study*, 2 CURRENT ENVTL. HEALTH REP. 423, 427 (2015); Anne Y. Oh et al., *Do Electronic Cigarettes Impart a Lower Potential Disease Burden Than Conventional Tobacco Cigarettes? Review on E-cigarette Vapor Versus Tobacco Smoke*, 124 LARYNGOSCOPE 2702, 2703–2705 (2014).

<sup>40</sup> Major tobacco companies that sell both cigarettes and e-cigarettes already have extensive smoker distribution lists and would be readily able to reach smokers through e-cigarette advertising sent directly only to pre-verified adult smokers and e-cigarette users. Applicant e-cigarette companies that did not have any such adult-smoker lists could obtain them from existing commercial sources or through promotions designed to secure the names and contact information of adult smokers. For more detail on how e-cigarettes could be marketed responsibly to increase switching by smokers while minimizing health-harming impacts, see Eric N. Lindblom, *Should FDA Try to Move Smokers to E-Cigarettes and Other Less-Harmful Tobacco Products and, If So, How?*, 73 FOOD & DRUG L. J. 276 (2018).

<sup>41</sup> A core assumption in this strategy is that it is much easier to minimize the risks of increasing health harms among those who would not otherwise initiate or relapse into any tobacco-nicotine use (e.g., by not exposing them to advertising and claims that cannot benefit them) than to try to develop research to convince FDA that allowing less-constraining public advertising and reduced-risk claims would be preferable because it would produce larger net public health gains (despite much larger risks of larger harms among innocents). Trying to develop lab research or simulated studies to show that the net public health benefit from such public and unconstrained reduced-risk advertising would still be positive (and acceptable) would be quite difficult and time consuming (and perhaps impossible) given the difficulties in predicting responsive market competition and consumer behaviors, and the many other factors that would be at play in both the near and long term. There could also be a strong aversion at FDA and elsewhere to allowing larger harms to innocents (especially children) to secure larger net public health gains. See, e.g., FDA Statement, *Statement from FDA Commissioner Scott Gottlieb, M.D., on meetings with industry related to the agency's ongoing policy commitment to firmly address rising epidemic rates in youth e-cigarette use* (October 31, 2018) [“[To] fulfill the central premise of our public health mandate – we may need to take actions that might narrow the off-ramp from smoking for adults in order to close the on-ramp to nicotine addiction to kids. Achieving the right balance requires a strong regulatory process that protects our nation’s youth.”], <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm624657.htm> (last visited Nov. 13, 2018).

(5) *For obtaining an MRTP order, propose a clearly accurate and reasonable claim of reduced-risk compared to smoking, for delivery only to adult current smokers, which would also state that: (a) the risk reductions can be secured only by sustained complete switching, (b) any e-cigarette use except as a smoking substitute increases harms, (c) e-cigarette use is not benign, (d) dual use can increase health harms and risks (if it does not accelerate smoking or total cessation), and (e) the most powerful way to minimize health harms and risks is to quit all tobacco-nicotine use.* Delivering the reduced-risk message only to smokers, as described in item (4), would target only those who could benefit from receiving them and make it less likely that the reduced-risk messages would prompt youth or former smokers to initiate. Including the additional information in (a) to (e) would also encourage only health-helping uses of e-cigarettes and discourage youth and former-smoker initiation, while also discouraging smokers who would otherwise quit from using the e-cigarette, instead, and discouraging smokers from engaging in long-term dual use instead of switching completely.<sup>42</sup>

(6) *Based on the above, provide as strong and compelling an analysis as possible to show that allowing the e-cigarette to enter or stay on the market and to be marketed with reduced-risk claims, as proposed, would be highly unlikely to produce any net public health loss of any significance and would very likely produce a significant net public health gain.* Developing this analysis would be greatly simplified by taking steps (1) through (5). For example, the analysis could point out that far more smokers would directly receive the reduced-risk claims encouraging them to switch (or quit all use) compared to the number of non-smoking youth or adults or former smokers who would be indirectly exposed to the e-cigarette's advertising and reduced-risk claims (which would also discourage non-switching use). Similarly, because the vast majority of smokers want to quit, but only a tiny fraction do so successfully each year, directing the reduced-risk claim to smokers would reach many more smokers who could benefit from switching and might do so than smokers who would otherwise quit and might be deferred from doing so—and the messaging would encourage helpful switching by the former and discourage any harmful switching by the latter.<sup>43</sup> Some relatively simple

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<sup>42</sup> The proposed marketing and delivery restrictions for the applicant e-cigarette and its reduced-risk claims would prevent youth at high-risk of becoming regular smokers from directly receiving or being directly exposed to the reduced-risk claims, which might help to prompt them to initiate into regular e-cigarette use instead of smoking. But such high-risk users are much more likely to have adult smoker family members and friends; so they would be more likely both to receive the e-cigarette reduced-risk claims secondhand and to be exposed to the modeling effects of adults switching from smoking to using the e-cigarettes. See, e.g., Kathrin Schuck et al., *Bidirectional Influences Between Parents and Children in Smoking Behavior: A Longitudinal Full-Family Model*, 15 *NICOTINE & TOBACCO RES.* 44, 47–48 (2013).

<sup>43</sup> In any given year, close to 70 percent of all smokers say they are interested in quitting, but only about 50 percent actually try to do so, and only about six percent successfully quit for at least six months. Stephen Babb et al., *Quitting Smoking Among Adults—United States, 2000–2015*, 52 *MORBIDITY & MORTALITY WKLY. REP.* 1457, 1457 (2017). Accordingly, the e-cigarette ads and relative-risk messaging would reach more than 10 smokers trying or intending to quit who would otherwise fail (and could,

modeling, based on the most conservative assumptions about relative harmfulness, could illustrate what a small proportion of the many smokers directly receiving the reduced-risk claims would need to switch to secure significant net health gains, even if surprisingly large portions of otherwise non-user youth and otherwise non-relapsing former smokers who might also be exposed to the claims began using the e-cigarette (with some smaller portion moving on to smoking).

(7) *Make a solid, good-faith effort to provide all the other information the Tobacco Control Act requires in the new-product and MRTTP applications.* It is the Tobacco Control Act, not FDA, that establishes the requirements for the applications and the standards for review. In particular, FDA's guidance documents relating to applications for new product and MRTTP orders are only FDA's recommendations and they are not legally binding.<sup>44</sup> Similarly, FDA requests for additional information from applicants might go well beyond the scope of what the Act requires or what is adequate to support a favorable FDA order.

Section 910 of the Tobacco Control Act states that new-product applications shall "be determined on the basis of well-controlled investigations, which may include 1 or more clinical investigations by experts qualified by training and experience to evaluate the tobacco product."<sup>45</sup> But the application could remind FDA that section 910 also explicitly states that such clinical investigations need to be used only "when appropriate" and that such extra-high-quality research need not be submitted if FDA determines that other valid scientific evidence is sufficient to evaluate the application.<sup>46</sup> The Act does not define "scientific evidence," but it certainly includes studies published in peer-reviewed research journals, as well as straight forward modeling based on conservative research-based assumptions. Section 911, governing MRTTP applications, does not explicitly require scientific evidence (nor mention

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therefore, only benefit from receiving them) for every single smoker it reached who would otherwise quit successfully (and who might still do so).

<sup>44</sup> FOOD & DRUG ADMIN., Draft Guidance: Premarket Tobacco Product Applications for Electronic Delivery Systems (May 2016) is still only in draft form and specifically states: "This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. *You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.*" *Id.* at 1 (emphasis added). See, also, FOOD & DRUG ADMIN., (March 2012) at Draft Guidance: Modified Risk Tobacco Product Applications 1; FOOD & DRUG ADMIN., Draft Guidance: Applications For Premarket Review of New Tobacco Products (Sept. 2011) at 1. All of FDA's final tobacco control guidance documents issued to date also include the same kind of text about not being legally binding. *Guidance*, FOOD & DRUG ADMIN., [www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm281147.htm](http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm281147.htm) [https://perma.cc/B499-G8EL] (last accessed Nov. 16, 2018).

<sup>45</sup> TCA, *supra* note 7, at § 910(c)(4), 21 U.S.C. § 387j(c)(4).

<sup>46</sup> *Id.*

clinical investigations),<sup>47</sup> but the evidentiary requirements for section 910 new product orders likely apply equally to new-product MRTPs.<sup>48</sup>

(8) *Commit to careful post-marketing surveillance and to stopping all relative-risk communications—or even withdrawing the e-cigarette from the market—if any solid evidence appears that the product or claims are producing any new net public health harms.* Section 911 specifically requires post-marketing surveillance for MRTP products, anyway (although section 910 does not).<sup>49</sup> For this proposed approach, the goal is to make sure the application describes what specific surveillance will be done and what remedial steps would be taken to assure FDA that any unexpected net public health losses prompted by the new product's availability or any related relative-risk claims would be quickly noticed and nipped in the bud. Among other commitments, the application could state that the manufacturer would immediately withdraw any specific flavored version of the subject e-cigarette allowed by the order if post-market surveillance showed that flavored version becoming disproportionately popular among youth, compared to adult smokers, or among youth at low-risk of becoming smokers, compared to high-risk youth or adult smokers.

(9) *Notify FDA that you want the application considered promptly, as is.* The submitted application should make as compelling a case as possible for issuing the order(s) as the e-cigarette company can develop in a reasonable time given its available resources. It should be supported primarily by published research, basic product information, and the application's proposed reduced-risk claims and restrictions on marketing. The applicant should ask FDA to identify any procedural or technical problems with the application so that they can be quickly remedied. The applicant should also quickly accept any revised or additional requirements or restrictions FDA proposes for the marketing of the e-cigarette or for the delivery or content of the reduced-risk claims that FDA believes would better promote and protect the public health (unless they

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<sup>47</sup> TCA, *supra* note 7, at § 911(g)(1), 21 U.S.C. § 387j(g)(1).

<sup>48</sup> For certain limited reduced-exposure claims that cannot meet the standards of the primary MRTP order pathway at section 911(g)(1), section 911(g)(2), allows FDA to issue a permissive MRTP order even when “scientific evidence is not available and, using the best available scientific methods, cannot be made available without conducting long-term epidemiological studies,” so long as “the scientific evidence that is available . . . demonstrates that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies.” 21 U.S.C. § 387j(g)(2). While this secondary pathway might appear easier (if a manufacturer would be content making only reduced-exposure claims), it also requires that “testing of actual consumer perception shows that, as the applicant proposes to label and market the product, consumers will not be misled into believing that the product—(I) is or has been demonstrated to be less harmful; or (II) presents or has been demonstrated to present less of a risk of disease than 1 or more other commercially marketed tobacco products.” TCA, *supra* note 7, at § 911(g)(2)(B)(iii), 21 U.S.C. § 387j(g)(2)(B)(iii). Establishing that for a reduced-exposure claim might be more difficult than showing that an explicit reduced-risk claim delivered just to smokers is accurate and not misleading. In both cases, the applicant would also have to show that delivering the claim would not produce any net harm to the health of the population as a whole.

<sup>49</sup> TCA, *supra* note 7, at § 911(i), (g)(2)(C)(ii), 21 U.S.C. § 387j(i), (g)(2)(C)(ii)]. *Id.* § 910(c)(4) [21 U.S.C. § 387j(c)(4)].

make marketing the product with any reduced-risk claims impossible). But strenuous efforts should be made to avoid being sucked into a relentless cycle of substantive FDA requests for clarification and new information and analysis, with the clock for a final decision starting at zero every time the application is altered or supplemented. If the application has been done right, following steps (1) to (8), FDA should not need anything more from the applicant to make an informed decision. Accordingly, any FDA requests for additional substantive evidence or analysis—unless clearly reasonable, appropriate, and helpful—should be refused. Instead, the applicant should ask FDA for a prompt decision based on the submitted application.<sup>50</sup>

(10) *If FDA does not issue an order in a reasonable time, challenge the delay in court.* The Tobacco Control Act requires FDA to issue new-product orders (positive or negative) within 180 days of receiving the applications.<sup>51</sup> But FDA can delay starting that clock until the application is deemed complete and can re-start the clock every time the manufacturer adds any significant new information or analysis into the application or makes any other significant changes.<sup>52</sup> The Act provides no specific timeframe for MRTTP orders, but seems to anticipate prompt action (e.g., requiring FDA to refer applications to the Tobacco Products Scientific Advisory Committee, which must respond with its recommendations within 60 days).<sup>53</sup> More importantly, FDA cannot justify taking a long time to issue an order if the application, following steps (1) to (8), is relatively short and to the point (tens or hundreds of pages, not thousands or millions) and the applicant has formally stated that its application is complete and ready for FDA's review and decision.<sup>54</sup>

(11) *If FDA rejects the application or issues an order denying the application, challenge the FDA action in court.* To win in court, the applicant would need to show that its application provided all the information required by the Act and made such a strong case that it would

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<sup>50</sup> Both section 910 and section 911 state that the applications shall, among other things, include such other information as FDA may require. TCA, *supra* note 7, at §§ 910(b)(1)(G), 911(d)(7) [21 U.S.C. § 387j(i)(b)(1)(G), (k)(d)(7)]. But that does not authorize FDA to require irrelevant or unnecessary information or go beyond the clear scope of the statute; and it likely authorizes FDA to establish new application requirements only through notice-and-comment rulemaking and only if they are consistent with the statute's language and purpose. In any case, the TCA clearly does not authorize FDA staff to establish new requirements for what applicants must submit, on a case-by-case basis, after the applications have been submitted, or before FDA will consider the application complete and begin considering it. If a manufacturer states that it considers its application complete and adequate and refuses to make additional changes or additions, all FDA may do is consider the application and either reject it as incomplete or determine whether or not to grant a permissive order.

<sup>51</sup> TCA, *supra* note 7, at § 910(c)(1) [21 U.S.C. § 387j(c)(1)].

<sup>52</sup> See, e.g., FOOD & DRUG ADMIN., Draft Guidance: Premarket Tobacco Product Applications for Electronic Delivery Systems (May 2016), at 10-11.

<sup>53</sup> TCA, *supra* note 7, at § 911(f) [21 U.S.C. § 387k(f)].

<sup>54</sup> Filing and pursuing lawsuits can be expensive. But asking a court to require that FDA move more quickly to make a summary judgment ruling on an application the applicant says is complete and ready for decision would be relatively straightforward and inexpensive. It is also possible that simply threatening or filing the lawsuit would spur FDA to move more quickly.

be “arbitrary, capricious, [or] an abuse of discretion” for FDA to reject the application or issue an order denying the application.<sup>55</sup> The Administrative Procedures Act standard gives regulatory agencies considerable deference, but the agency must still articulate a satisfactory explanation for its decision, and there must be a rational connection between the facts and the agency’s choices.<sup>56</sup> An application that carefully followed steps (1) through (8) would represent a rigorous, good-faith effort by the applicant to structure its e-cigarette to minimize its harmfulness and youth attractiveness and to design and target its marketing and relative-risk claims directly at prompting health-improving switching by smokers while minimizing the risk of prompting any health-harming impacts. Accordingly, a court might find FDA’s denial of the application arbitrary or capricious because it would be difficult, if not impossible, to imagine what more an e-cigarette company (or any other tobacco product manufacturer) could do to submit an application FDA would accept—and the Act would not have included new product and MRTP provisions unless it intended that manufacturers be able to obtain new product and MRTP orders.

FDA could claim that more research is needed to determine exactly how much less harmful the e-cigarette is for users and exposed users compared to smoking. But the application would have already shown that the e-cigarette merits a permissive new product and/or MRTP order even if it turns out that it is as harmful as the most conservative reasonable estimate based on available research (or perhaps even if it is as harmful to users as smoking).

Similarly, FDA might claim that more research is needed to develop better estimates of how allowing the marketing of the e-cigarette with reduced-risk claims could impact different types of smoker and non-smoker behavior. But developing reliable projections will be extremely difficult and uncertain until some similar product with similar reduced-risk claims has actually been allowed on the market to develop real-world experience. In addition, an application following this strategy would have already done everything possible to focus the e-cigarette and its marketing directly at promoting health-improving behavior changes while minimizing related risks of prompting health-harming behavioral impacts. It also would have shown net public health benefits even if the resulting beneficial behavior changes were smaller than available evidence suggests they would be and the negative behavior changes were larger than expected. It is also clear from the Tobacco Control Act that if there were more that the applicant could have done to maximize health benefits and minimize health harms through its marketing of the e-cigarette and making the reduced-risk claims, FDA could have imposed those additional requirements in a permissive order rather than issuing a

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<sup>55</sup> Administrative Procedures Act, 5 U.S.C. § 706(2)(A) (2011); TCA, *supra* note 7, at § 912(b) [21 U.S.C. § 3871].

<sup>56</sup> F.E.R.C. v. Elec. Power Supply Ass’n, 136 S. Ct. 760, 782 (2016).

negative order.<sup>57</sup> In this context, any FDA claim that no permissive order could be issued because of a need for longer-term studies and clinical investigations would indicate that no MRTP orders could possibly be issued until years or even decades from now, which the courts would not likely accept.<sup>58</sup>

## DISCUSSION AND CONCLUSION

Some might be skeptical that this relatively simple, straight-forward approach to securing permissive new product and MRTP orders could work. But giving this strategy a try would not be enormously expensive or take much time, especially when compared to the applications that manufacturers of other types of tobacco products have submitted to FDA. Moreover, even if FDA rejected the application and the courts upheld FDA's decision, the final court ruling would likely provide increased clarity about exactly what the new-product and MRTP application procedures do and do not require from applicants, what FDA can and cannot require applicants to do after an application is submitted, how quickly FDA must issue orders, how the statutory standards for evaluating applications should be interpreted and applied, and how applicants could submit successful applications.<sup>59</sup>

Others might reject this strategy as accepting and incorporating what they consider excessive restrictions on e-cigarettes and their marketing, either from a general dislike of business constraints or because some of the proposed restrictions might go beyond just preventing the e-cigarette's marketing from increasing health-harming new use but also impede its ability to prompt beneficial switching by current and otherwise future smokers. But the proposed restrictions, which err on the side of reducing the risk that the e-cigarette's marketing or reduced-risk claims would cause brand-new health harms, are all likely needed to produce an application that FDA might accept relatively quickly (or be required by the courts to accept) as "appropriate for the protection of the public health." And obtaining the first favorable FDA new product

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<sup>57</sup> TCA, *supra* note 7, at §§ 910(c)(2), 911(h) [21 U.S.C. § 387j(c)(2) & k(h)].

<sup>58</sup> Although legally challenging a negative FDA new product or MRTP order might be more complicated than asking a court to require FDA to take action after a reasonable time period had already elapsed, it would still be relatively straight forward. The e-cigarette company could simply provide the court with a copy of its final application and the order denying it; state that FDA's denial was arbitrary or capricious given the facts and analysis in the application and the order; and ask the court to make a summary judgment ruling based on that information.

<sup>59</sup> Some might say that adopting the approach proposed here is unnecessary or premature given recent FDA announcements that FDA hopes "to ensure that there's a clear viable pathway to seek FDA [new product] authorization," is committed to developing new guidance and regulations that will "better spell out the rules of the road for industry" of the regulatory process for electronic nicotine delivery systems and other products, especially in regard to improving the efficiency and transparency of the new product review process, and plans to announce additional improvements to the product application and review processes. FDA Statement, *Statement from FDA Commissioner Scott Gottlieb, M.D., on agency's ongoing commitment to improving efficiency, transparency of tobacco product application review process as part of FDA's comprehensive framework to reduce tobacco-related disease and death* (October 22, 2018), <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm623949.htm>, last accessed Nov. 16, 2018. However, while those statements by FDA Commissioner Gottlieb suggest that FDA might make the application processes for seeking new product and MRTP orders more understandable and perhaps more streamlined and efficient, the Commissioner also said that "FDA expects that manufacturers will develop *higher quality and more complete applications*, as the agency continues to explore clear and meaningful measures to make tobacco products less toxic, appealing and addictive." *Id.* (emphasis added).



and MRTP orders for e-cigarettes, no matter how restrictive is a critically important first step toward possibly obtaining more flexible or permissive new product or MRTP orders in the future.

Right now, no companies selling e-cigarettes have even submitted applications to market e-cigarettes with reduced-risk claims. Nor has any e-cigarette company submitted or received a new product order. So, what is needed to obtain such orders remains unclear. Compared to doing nothing or submitting massive, expensive applications, this strategy offers a relatively simpler way for e-cigarette companies to take the initiative and move things forward. To follow this strategy, they would need to take the public health goals of the Tobacco Control Act very seriously and do everything they can to ease any concerns at FDA that issuing a permissive order might backfire and produce net public health harms instead of net gains (even if that might reduce the size of the potential overall net public health gains). That means accepting some major restrictions on the applicant e-cigarette and its marketing and reduced-risk claims. But accepting those limitations should pave the way for actually getting new e-cigarettes onto the market legally and actually being allowed to make MRTP claims—which would provide important insights into what manufacturers must show in the new product applications all existing e-cigarettes must submit to stay on the market.

In addition, an application pursuant to this strategy, whether successful or not, would not have any effect on what other e-cigarettes already on the U.S. market with FDA's consent are or are not allowed to do. Nor would a permissive order establish requirements all other e-cigarettes would have to meet. The door would still be open to applications proposing less restricted products, marketing, and reduced-risk claims (if they could meet the applicable standards, which would remain unchanged). On the other hand, an order allowing an e-cigarette following this strategy to enter the market with reduced-risk claims would produce, for the first time, real-world experience and evidence regarding the impacts from such reduced-risk marketing on smoker and other consumer behavior and related health impacts. That would provide direct insights and guidance regarding how subsequent new product or MRTP applications might also meet the Act's public health standards and secure permissive orders while proposing less strict product or marketing restrictions or different relative-risk messaging.

For too long, members of the tobacco industry, especially e-cigarette companies, have been complaining about the FDA new-product and MRTP order pathways but not doing anything about it. The very few companies that have made attempts to obtain new-product or MRTP orders for less-harmful tobacco products (all major tobacco companies with extensive resources) have tried to persuade FDA by providing hundreds of thousands of pages of research, data, and analysis and then providing thousands more in response to FDA requests for clarification or more information. By assuming there is no other way to proceed, the tobacco industry is promoting and accepting a complex, expensive, slow, and cumbersome process—and perhaps helping to lock it in place. So far, no e-cigarette manufacturers have tested the new-product or MRTP procedures to find out whether much simpler, streamlined applications might work.<sup>60</sup>

The strategy presented here offers an effective way manufacturers of e-cigarettes could do that. In the worst case for a manufacturer, trying this strategy would confirm that the procedures for obtaining new-product or MRTP orders are as bad as the

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<sup>60</sup> *Tobacco Product Marketing Orders*, *supra* note 10. *Modified Risk*, *supra* note 9.

industry has alleged and feared, setting the stage for possible legislative changes. As outlined above, however, following this strategy is more likely to show that the existing procedures offer a reasonably expedient way for thoughtful manufacturers to obtain the orders they need to implement truly effective harm-reducing product innovations or to make reduced-risk product claims that will actually benefit the public health—or at least will do so once the courts have weighed in. Either way, following this strategy would be much more productive than doing nothing, a lot less expensive and time consuming than the MRTP applications filed to date, and more likely to produce helpful results both for the manufacturers and the public health.<sup>61</sup>

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<sup>61</sup> This paper tries to prompt constructive action by companies that sell e-cigarettes or other non-combusted tobacco products that will not only benefit their bottom line but help to protect and promote the public health. It can be seen as a complement or alternative to an FDA-directed strategy to move smokers who will not otherwise quit to less-harmful tobacco products. For more on that approach, see Eric N. Lindblom, *Should FDA Try to Move Smokers to E-cigarettes and Other Less-Harmful Tobacco Products and, If So, How?*, 73 *FOOD & DRUG L. J.* 276 (2018). FDA might also follow a process that roughly parallels the one proposed here in its development and implementation of new tobacco control rules to get them implemented, through judicial view, and successfully in place more quickly.