DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Premarket Tobacco Product Applications and Recordkeeping Requirements

Docket No. FDA-2019-N-2854

Preliminary Regulatory Impact Analysis
Initial Regulatory Flexibility Analysis
Unfunded Mandates Reform Act Analysis

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I. Introduction and Summary

A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, Executive Order 13771, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Executive Order 13771 requires that the costs associated with significant new regulations "shall, to the extent permitted by law, be offset by the elimination of existing costs associated with at least two prior regulations." We believe that this proposed rule is not an economically significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the proposed rule, if finalized, would generate net benefits or negligible costs for most affected small entities, we propose to certify that the proposed rule would not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $154 million, using the most current (2018) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Summary of Costs and Benefits

The proposed rule, if finalized, would add a requirement that tobacco manufacturers of grandfathered tobacco products and products that are exempt from the requirements of demonstrating substantial equivalence maintain records to demonstrate that they can legally market their products. For products that receive a Premarket Tobacco Product Application (PMTA) marketing order, the proposed rule, if finalized, would require certain postmarket reporting, including periodic reporting and adverse experience reporting. The proposed rule also establishes requirements for the content and format of PMTA and the procedures we follow to review the PMTA.

If finalized, the proposed rule would create cost savings for firms and for us by reducing the number of follow-on submissions for PMTAs. The proposed rule would also create cost savings for us by reducing the cost of review, reducing the number of deficiency letters we would issue during substantive scientific review, and eliminating the need to process unnecessary data. In Table 1, we present the total benefits of the proposed rule. We estimate that average annualized benefits over 20 years would equal $5.54 million at a 7 percent discount rate and $5.44 million at a 3 percent discount rate.

If finalized, the proposed rule would create costs for firms and for us by increasing the number of complete PMTA submissions for deemed and originally regulated tobacco products. Moreover, because this is the first regulation to account for the costs of the PMTA requirements for originally regulated products, we also include the costs to submit and review PMTAs for these tobacco products; we already included the costs to submit and review PMTAs for deemed tobacco products in the final regulatory impact analysis for the Deeming Rule. Firms would incur costs to maintain and submit postmarket reports, and we would incur costs to review postmarket reports. Finally, firms would incur costs to read and understand the rule and costs to maintain records for some grandfathered products. In Table 1, we present the total costs of the proposed rule. We estimate that average annualized costs over 20 years would equal $7.05 million at a 7 percent discount rate and $6.76 million at a 3 percent discount rate.

Table 1. Summary of Benefits, Costs, and Distributional Effects of the Proposed Rule

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized ($m/year)	$5.54	$2.57	$9.23	2017	7%	20 years	All quantified benefits are cost savings.
		$5.44	$2.54	$9.03	2017	3%	20 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Costs	Annualized Monetized ($m/year)	$7.05	$3.18	$11.65	2017	7%	20 years	
		$6.76	$3.12	$11.05	2017	3%	20 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized ($m/year)							
		From:			To:			
	Other Annualized Monetized ($m/year)							
		From: Products without marketing orders.			To: Products with marketing orders.			
Effects	State, Local, or Tribal Government: None Small Business: None Wages: None Growth: None							

In line with Executive Order 13771, in Table 2 we estimate present and annualized values of costs and cost savings over an infinite time horizon.

Table 2. EO 13771 Summary Table (in $ Millions 2016 Dollars, Over an Infinite Time Horizon)[a]

	Primary Estimate (7%)	Lower Bound (7%)	Upper Bound (7%)	Primary Estimate (3%)	Lower Bound (3%)	Upper Bound (3%)
Present Value of Costs	$104.04	$47.84	$170.31	$214.04	$101.20	$349.33
Present Value of Cost Savings	$83.18	$38.76	$138.98	$177.26	$82.15	$296.89
Present Value of Net Costs	$20.86	($0.23)	$44.29	$36.78	($14.19)	$91.71
Annualized Costs	$3.03	$1.39	$4.96	$6.23	$2.95	$10.17
Annualized Cost Savings	$2.42	$1.13	$4.05	$5.16	$2.39	$8.65
Annualized Net Costs	$0.61	($0.01)	$1.29	$1.07	($0.41)	$2.67

[a] Only the primary estimates (mean) sum in simulation results.

C. Terminology

In Table 3, we provide definitions for several terms we use in this document. We note that these definitions only apply to this document.

Table 3. Terms used in the Regulatory Impact Analysis

Term	Description
We, our, us	We use these terms to refer to the United States Food and Drug Administration.
ENDS	"ENDS" refers to electronic nicotine delivery systems and includes devices, components, and/or parts that deliver aerosolized e-liquid when inhaled. Generally, ENDS are noncombustible tobacco products, including e-cigarettes and e-liquids.
E-Cigarette	An e-cigarette refers to an electronic device that delivers e-liquid in aerosol form into the mouth and lungs when inhaled; it is also referred to as an aerosolizing apparatus. For example, we consider vapes or vape pens, personal vaporizers, cigalikes, e-pens, e-hookahs, e-cigar, and e-pipes to be e-cigarettes. E-cigarettes may either be open e-cigarettes or closed e-cigarettes. An open e-cigarette, also referred to as a refillable e-cigarette, is an e-cigarette that includes a reservoir that a user can refill with an e-liquid of their choosing. A closed e-cigarette is an e-cigarette that includes an e-liquid reservoir that is not intended to be refillable, such as a disposable cigalike, or that uses e-liquid contained in replaceable cartridges or pods that are not intended to be refillable. If an e-cigarette contains e-liquid it is referred to as a prefilled e-cigarette. The term e-cigarette in this analysis corresponds to the term "delivery system" used in the regulatory impact analysis for the Final Deeming Rule.

E-Liquid	E-liquids are a type of ENDS product and generally refer to liquid nicotine and nicotine-containing e-liquids (i.e., liquid nicotine combined with colorings, flavoring, and/or other ingredients). Liquids that do not contain nicotine or other material made or derived from tobacco, but that are intended or reasonably expected to be used with or for human consumption of a tobacco product, may be components or parts, and, therefore, subject to our tobacco control authorities.
Originally Regulated Product	As described in Table 4, originally regulated products include cigarettes, cigarette tobacco, smokeless tobacco, and roll-your-own tobacco.
PMTA Bundle	A PMTA bundle is a set of individual PMTAs submitted at the same time for which the costs of submission and the costs of review overlap substantially. For example, varieties of a product may each require separate PMTAs, but firms can rely on many of the same studies for these PMTAs, and we can review these PMTAs as a group. The term PMTA bundle in this analysis corresponds to the term "PMTA application process" used in the regulatory impact analysis for the Final Deeming Rule.
Original Bundle	An original bundle is a set of PMTAs for new tobacco products that are not modifications to products with existing marketing orders. The term "original" in this analysis corresponds to the term "initial" in the regulatory impact analysis for the Final Deeming Rule.
Supplemental Bundle	In this analysis, a supplemental bundle refers to a set of supplemental PMTAs. Supplemental PMTAs are PMTAs for new tobacco products that are modifications to products with existing marketing orders. Subject to the conditions described in this proposed rule, applicants may satisfy PMTA content requirements by cross-referencing previously reviewed PMTAs. The term "supplemental" in this analysis corresponds to the term "subsequent" in the regulatory impact analysis for the Final Deeming Rule.
Resubmission	A resubmission is another PMTA format that applicants who are seeking a marketing order for a tobacco product would use to respond to deficiencies outlined in a no marketing order. An applicant may submit a resubmission for the same tobacco product that received a no marketing order or for a different new tobacco product that results from changes necessary to address the deficiencies outlined in the no marketing order. Subject to the conditions described in this proposed rule, applicants may satisfy PMTA content requirements by cross-referencing previously reviewed PMTAs. Firms may not use the abbreviated resubmission format for bundles that we refused to accept or refused to file, or for bundles that were withdrawn during review.
Initial Submission	An initial submission is the first submission of a given product bundle. This includes first submissions of original bundles and first submissions of supplemental bundles.

Initial Review	We use this term to refer to our review of an initial submission.
Follow-On Submission	We use the term "follow-on" submissions in this analysis to refer to any second submission for a given product bundle. In our analysis, follow-on submissions may include the second submissions for products that we refused to accept or refused to file, or a resubmission of a PMTA as defined in this table of terms.
Follow-On Review	We use this term to refer to our review of a follow-on submission.
Acceptance Review	The first stage of our review of a PMTA is acceptance review. Following acceptance review, we may accept or refuse to accept the PMTA. Accepted PMTAs continue to filing review, while we end our review of PMTAs that we refuse to accept.
Filing Review	The second stage of our review of a PMTA is filing review. After we accept a PMTA for review, we conduct a filing review to determine whether the application contains sufficient information to permit a full substantive review of the application. Following filing review, we may file or refuse to file the PMTA. Filed PMTAs continue to substantive review, while we end our review of PMTAs that we refuse to file.
Substantive Review	The third and final stage of our review of a PMTA is substantive review. During substantive review, we determine whether there are no grounds for a denial of a marketing order as described in the proposed rule. We issue marketing orders for products that meet this standard, and we issue no marketing orders for products that do not meet this standard.
Marketing Order	A marketing order authorizes a new tobacco product to be introduced or delivered for introduction into interstate commerce.
No Marketing Order	A no marketing order states that a product may not be introduced or delivered for introduction into interstate commerce.
Deficiency Letter	A deficiency letter is a request from us to an applicant for an amendment to a PMTA. These letters pause the review clock, delaying the review of a PMTA.
Incomplete Bundle	We call a bundle "incomplete" if we complete our review of that bundle with acceptance review. Incomplete bundles include bundles that we refuse to accept in our review and bundles that firms withdraw during acceptance review.
Partially Complete Bundle	We call a bundle "partially complete" if we complete our review of that bundle with filing review. Partially complete bundles include bundles that we refuse to file in our review and bundles that firms withdraw during filing review.
Complete Bundle	We call a bundle "complete" if we complete our review of that bundle with substantive review.
Deeming Rule	The final rule that deemed tobacco products not originally covered by the TCA, including cigars, pipe tobacco, waterpipe tobacco, ENDS, and other novel tobacco products, to also be subject to the tobacco product restrictions in the FD&C Act[1] (Ref. 1).
Deeming Compliance Period (DCP)	A recent court ruling vacated our existing compliance policy for premarket review of combustible deemed tobacco products. As of the publication of this rulemaking, we are uncertain about how our compliance policy will change. For the purposes of this analysis, we

[1] Chapter IX of the FD&C Act.

	assume that noncombustible deemed products will comply with the Deeming Rule by submitting premarket applications by the end of 2020.
Post-Deeming Compliance Period (Post-DCP)	Refers to the years following the initial Deeming compliance period. For the purposes of this analysis, we assume that the post-DCP period begins in 2021.

II. Preliminary Regulatory Impact Analysis

A. Background

1. Marketing Tobacco Products

The Tobacco Control Act[2] (TCA) established requirements for premarket authorization of new tobacco products (Ref. 2). We do not require premarket authorization for some tobacco products. We call these products "grandfathered" tobacco products. A grandfathered tobacco product is a tobacco product that manufacturers commercially marketed in the United States on February 15, 2007.

A new tobacco product is any tobacco product (including those products in test markets) that was not commercially marketed in the United States on February 15, 2007 or any modification of a tobacco product where the modified tobacco product was commercially marketed after February 15, 2007. Generally, to market a new tobacco product, manufacturers must obtain marketing authorization through one of three premarket review pathways:

1) Premarket tobacco product applications[3] (PMTA pathway);
2) Applications intending to demonstrate that the new tobacco product is substantially equivalent to a predicate tobacco product[4] (SE pathway);
3) Requests for an exemption from the requirement of demonstrating substantial equivalence[5] (SE Exemption Request pathway)

Manufacturers may submit a PMTA for any new tobacco product. To receive marketing authorization through the PMTA pathway, a manufacturer must show, among other criteria, that permitting the marketing of the new tobacco product would be appropriate for the protection of public health.[6]

We review submissions through the PMTA pathway to determine whether to issue a marketing order for new tobacco products. Once we issue a marketing order, manufacturers may introduce that tobacco product into interstate commerce.

[2] The Family Smoking Prevention and Tobacco Control Act of 2009, also called the Tobacco Control Act, amended the Federal Food, Drug, and Cosmetic Act (FD&C Act), giving us the authority to regulate tobacco products under Chapter IX of the FD&C Act.
[3] Section 910(b) of the FD&C Act.
[4] Section 905(j) of the FD&C Act.
[5] Section 905(j)(3) of the FD&C Act.
[6] Section 910(c) of the FD&C Act.

2. Premarket Tobacco Product Applications

To issue a marketing order for a new tobacco product through the PMTA pathway, we need sufficient information to find that:

1) Permitting the marketing of the new tobacco product would be appropriate for the protection of public health;
2) Firms manufacture the new tobacco product in accordance with tobacco product manufacturing practice regulations (TPMP)[7];
3) The new tobacco product's labeling is not false or misleading;
4) The new tobacco product complies with applicable product standards.[8]

We have issued a guidance on PMTAs for electronic nicotine delivery systems (ENDS), which describes the contents of PMTAs required by statute (Ref. 3). We also suggest general recommendations for additional information that would help us review such PMTAs.

3. Types of Tobacco Products

In Table 4, we list some of the common types of tobacco products on the market in the United States. In the first column, we list "originally regulated tobacco products." The Tobacco Control Act gave us immediate authority to regulate cigarettes, cigarette tobacco, smokeless tobacco, and roll-your-own tobacco. Manufacturers of these products have been subject to premarket authorization requirements under the FD&C Act since the Tobacco Control Act became effective. In the next two columns we include deemed tobacco products. The Deeming Rule requires that manufacturers obtain premarket authorization before marketing new cigars, pipe tobacco products, waterpipe tobacco products, ENDS, or other novel tobacco products.

Table 4. Common Types of Tobacco Products

Originally Regulated Tobacco Products	Combustible Deemed Tobacco Products	Noncombustible Deemed Tobacco Products
Cigarettes Cigarette Tobacco Smokeless Tobacco Roll-Your-Own Tobacco	Cigars Pipe Tobacco Waterpipe Tobacco	Electronic nicotine delivery systems, including e-cigarettes and e-Liquids

B. Market Failure Requiring Federal Regulatory Action

Without regulatory action, tobacco manufacturers would only be able to refer to the FD&C Act and any existing guidance about our current expectations for PMTA content. This proposed rule would correct an institutional failure caused by inadequate information about our expectations for complete PMTAs. This failure creates inefficiencies in the process of premarket review that delay the marketing of products that we would potentially determine are appropriate for the protection of public health. An inefficient review process increases the premarket review

[7] Regulations would be issued under section 906(e) of the FD&C Act. However, we have not yet issued these regulations.

[8] Section 907 of the FD&C Act. If a new tobacco product deviates from an applicable product standard, then we also need adequate information to justify that deviation, if applicable.

costs for us and reduces profits for firms. The proposed rule, if finalized, would address these inefficiencies in premarket review process.

Tobacco products also have many characteristics that contribute to adverse health outcomes and consumers have incomplete information about such characteristics. For example, consumers may not learn of serious and unexpected adverse experiences caused by the consumption of specific tobacco products. Therefore, consumers often fail to internalize these adverse health outcomes when choosing to consume tobacco products.

With premarket review of a PMTA, we evaluate information from manufacturers to determine whether permitting the marketing of a new tobacco product would be appropriate for the protection of public health. Adding new reporting and recordkeeping requirements would allow us to more closely monitor marketed tobacco products, allowing us to identify characteristics that contribute to adverse health outcomes and enhancing our ability to protect public health. Similarly, adverse experience reports would provide us with necessary information to help determine whether the marketing of the product is no longer appropriate for the protection of public health. Consequently, improving premarket review and postmarket surveillance would help us avoid the market failure created by consumers' failure to internalize adverse health outcomes associated with the consumption of tobacco products.

C. Purpose of the Proposed Rule

The proposed rule, if finalized, would add a requirement that tobacco manufacturers of grandfathered tobacco products and products that are exempt from the requirements of demonstrating substantial equivalence maintain records to demonstrate that they can legally market their products. For products that receive a PMTA marketing order, the proposed rule would require certain postmarket record retention and reporting, including periodic reporting and adverse experience reporting. The proposed rule also establishes requirements for the content and format of PMTA and the procedures we follow to review the PMTA.

1. Recordkeeping Requirements

The proposed rule, if finalized, would require recordkeeping for tobacco manufacturers. This requirement applies to manufacturers of grandfathered products and products that are exempt from the requirements of demonstrating substantial equivalence. We would require that manufacturers of grandfathered products, tobacco products that manufacturers marketed commercially in the United States on February 15, 2007, maintain records demonstrating their grandfathered status. The proposed rule describes the types of records that manufacturers could use to demonstrate their grandfathered status. The rule would require that records be legible, in the English language, and available for inspection and copying by FDA employees. We would also require that manufacturers retain these records for four years from the date that:

- We make a grandfathered determination, or
- The manufacturer ceases introduction into interstate commerce, whichever occurs sooner.

The proposed rule would also establish recordkeeping requirements related to the SE Exemption Request pathway. The proposed rule would require that manufacturers that have submitted an abbreviated report[9], and received a letter from us acknowledging the receipt of an abbreviated report, maintain all records necessary to support the SE exemption. The proposed rule describes the type of records that we would require manufacturers to maintain for SE Exemption Request products. The proposed rule would not require a manufacturer to create new or additional records, rather it would require manufacturers to maintain all records that support its abbreviated report. We would require that manufacturers retain these records for four years from the time we issue an acknowledgement letter in response to the SE Exemption Request. In addition, the proposed rule would require manufacturers to maintain records demonstrating that the modification is to a legally marketed product, such as a grandfathered tobacco product or a new tobacco product that has satisfied premarket review requirements[10].

2. Postmarket Requirements

The proposed rule, if finalized, would require applicants to establish and maintain records and submit certain reports. We would require that applicants submit two types of reports after receiving a marketing order: periodic reports and serious and unexpected adverse experience reports. In general, while we may require in a specific marketing order that firms make reports more or less frequently, initially we expect to require periodic reports annually. These reports would include information about manufacturing, facilities, or control changes made during the reporting period, information on new studies and published literature, information about adverse experiences with the product, sales and distribution data for the reporting period, information about changes in labeling and advertising, and an assessment of the continued appropriateness of the product for the protection of public health.

We would also require firms with marketing orders through the PMTA pathway to submit reports for any serious and unexpected adverse experiences associated with the marketed tobacco product within 15 days of receiving or becoming aware of the adverse experience. These adverse experience reports would provide us with necessary information to help determine whether the marketing of the product is no longer appropriate for the protection of public health and whether the marketing order should be temporarily suspended. Currently firms can submit voluntary adverse experience reports for tobacco products. However, the proposed rule, if finalized, would make reporting mandatory.

3. PMTA Submissions

The proposed rule includes detailed content and format requirements for PMTAs, including the types of data and studies applicants should submit. However, we anticipate that the level of effort required to gather information and prepare the PMTA aligns with the effort described in the final regulatory impact analysis for the Deeming Rule (Ref. 4). Consequently, we do not expect that this proposed rule, if finalized, would change the costs of preparing and submitting a PMTA, relative to the cost estimates in the final regulatory impact analysis for the Deeming Rule. For new tobacco products that result from a modification or modifications to the original tobacco product that received a PMTA marketing order, the proposed rule would permit

[9] Section 905(j)(1)(A)(ii) of the FD&C Act.
[10] Section 910(a)(2) of the FD&C Act.

applicants to submit a less burdensome type of PMTA called a supplemental PMTA. For such modifications, we would allow manufacturers to cross-reference the PMTA for the original tobacco product in their supplemental PMTA.

For tobacco products that received no marketing orders, the proposed rule would permit applicants to resubmit the PMTA in an abbreviated form that addresses the deficiencies described in the no marketing order and cross-references the original PMTA. In this analysis, we refer to these resubmissions as follow-on submissions (see Table 3). Firms could not use an abbreviated format for PMTAs that we have refused to accept, refused to file, cancel, administratively closed, or for withdrawn PMTAs.

4. PMTA Review

Based on our current practices, the proposed rule describes in detail the procedures we would follow to review PMTAs. When an applicant submits a PMTA, we would conduct three levels of review, each more stringent than the previous level. With each level of review, we would determine if the applicant has provided sufficient detail in the appropriate format to proceed to the next level of review. The proposed rule, if finalized, would raise the bar for filing, so that we would only file those PMTAs that contain enough information for substantive review. Changing the standard for filing would improve the efficiency of review and incentivize firms to submit more complete PMTAs.

The time it takes to review a PMTA depends on the complexity of the product. We intend to act as quickly as possible for all new applications, while ensuring that we meet the statutory standards. Figure 1 summarizes the main steps in the review of PMTA bundles.

We expect our review would take 180 days from the receipt of the last piece of information needed to complete the PMTA. However, under the proposed rule, we also describe the types of events that could pause or restart the 180-day review period. For example, we may identify deficiencies in a PMTA during our review and request that firms submit additional information. Firms would then submit amendments to their PMTAs containing the required information. Under the proposed rule, we could pause the 180-day review period for minor amendments and restart the 180-day review period for major amendments.

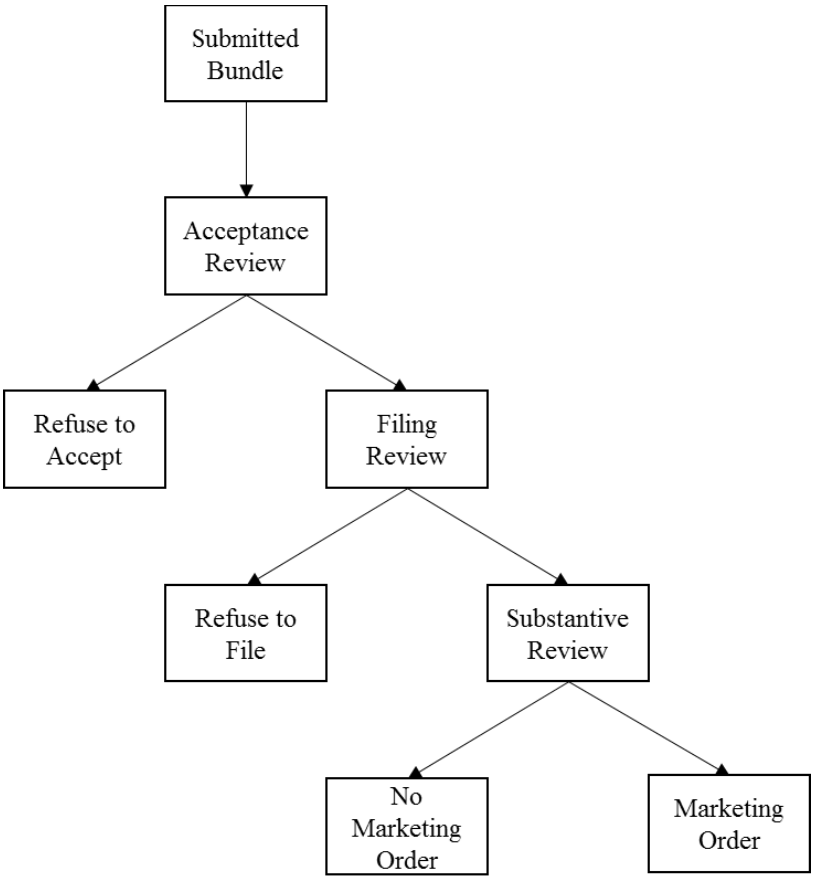

Figure 1. Overview of PMTA Review

D. Baseline Conditions

1. Description of the Baseline

The baseline for the proposed rule depends on the type of tobacco product. The final regulatory impact analysis for the Deeming Rule estimated the costs of submitting and reviewing PMTAs for deemed tobacco products (Ref. 4). Consequently, for this analysis we use a post-Deeming baseline for deemed tobacco products. Specifically, we update the cost to submit and review PMTAs used in the final regulatory impact analysis for the Deeming Rule by adjusting for inflation and changes in wage rates. We also consider updated data on market consolidation that has occurred since Deeming Rule published (see Section F.1 in Section V). Since the publication of the Deeming Rule, CTP's Office of Science has identified inefficiencies in the PMTA pathway for deemed tobacco products. We also incorporate the cost of these inefficiencies in PMTA submission and review in our baseline costs. We use the difference between the modified total costs from the Deeming Rule and the total costs in the presence of this rulemaking to estimate the incremental impacts of this proposed rule.

By contrast, the final regulatory impact analysis for the Deeming Rule did not capture the costs of submitting and reviewing PMTAs for originally regulated products that would receive marketing orders through the PMTA pathway. For originally regulated products the proposed

rule codifies the statutory requirements for PMTAs in the TCA. Consequently, for this analysis we use a pre-statutory baseline for originally regulated tobacco products. To capture costs attributable to the TCA, we assume that the proposed rule implements the statutory requirements for PMTAs described in the TCA for originally regulated tobacco products (see Table 36). In section I, we repeat our analysis using an alternative post-statutory baseline for originally regulated products.

2. The Cost of Labor

Throughout this analysis, we estimate the costs and cost savings from the proposed rule using the cost of labor. Following guidelines from the Department of Health and Human Services (Ref. 5), we estimate the cost of labor as the fully loaded wage, or the wage including benefits and overhead equal to 100 percent of the mean wage. For industry wages, we use 2017 mean wage estimates from the Bureau of Labor Statistics' National Industry-Specific Occupational Employment and Wage Estimates (Ref. 6) for the tobacco manufacturing industry. For staff from our Center for Tobacco Products (CTP) we use 2018 data from FDA's Fully Loaded Full Time Employee (FTE) Cost Model to estimate the fully loaded wage. Table 5 shows the values of the mean wages and the fully loaded wages used in this analysis.

Table 5. Wages Used to Evaluate the Cost of Labor

Occupation	Mean Wage	Fully Loaded Wage
Management	$59.84	$119.68
Lawyers	$64.11	$128.22
Administrative Staff	$19.73	$39.46
Scientists	$28.90	$57.80
Engineers	$45.32	$90.64
Composite Wage for Preparing PMTAs and Related Reports[11]	$36.48	$72.95
CTP Staff	$65.96	$119.18

Note: All wages are in 2017 dollars.

3. Inflation Adjustments

All cost estimates in this analysis are in 2017 dollars. We use GDP price indices from the Bureau of Economic Analysis to adjust for inflation. In Table 6, we show GDP price indices and the inflation factors for the different inputs that we adjust for inflation in this analysis.

Table 6. Inflation Factors for Inputs in the Analysis

Type of Input	Year of Estimate	GDP Price Index	Inflation Factor[a]
Costs of composition, design, and manufacturing studies, human studies, and toxicological studies for PMTAs (from the final regulatory impact analysis of the Deeming Rule)	2014	103.69	1.04

[11] Following the regulatory analysis for the Deeming rule, the composite wage is a weighted average of the wages for lawyers, administrative staff, scientists, and engineers.

Private sector wages	2017	107.93	1.00
Sales of ENDS products	2018	110.34	0.98
Wage for CTP staff	2018	110.34	0.98

[a] The inflation factor equals the GDP Price Index for 2017 divided by the GDP Price Index for the year of the estimate. To adjust a value for inflation, we multiply the value by the inflation factor.

4. Number of Potential PMTA Applicants

To estimate the number of potential PMTA applicants, we combine tobacco establishment registration data with information from Dun & Bradstreet (D&B). We estimate that there are currently approximately 2,450 firms with registered tobacco establishments, representing approximately 3,400 establishments. Firms that only own vape shop establishments represent approximately 750 of the 2,450 firms, or 1,500 of the 3,400 establishments. According to the D&B data, about 84 percent of the firms registered with FDA have fewer than 1,500 employees.[12]

5. Types of PMTAs

a. Types of Products

We assume that firms would only submit PMTAs for deemed e-liquids and e-cigarettes and we assume that cigars and other deemed tobacco products would utilize other marketing pathways. This assumption is consistent with the regulatory impact analysis for the Deeming rule. Furthermore, given the pre-statutory baseline for originally regulated tobacco products, we assume that firms would not submit PMTAs for any originally regulated tobacco products in the baseline.

b. PMTA Bundles

Although firms must submit PMTAs for individual products, firms often conduct studies and gather existing research for related products. Some of the costs to prepare and submit applications overlap significantly for products. We permit a bundled submission for PMTAs that contain overlapping information. Therefore, we estimate costs at the PMTA bundle level, where a PMTA bundle is a set of PMTAs contained within a single submission. For our analysis, we assume that firms submit all PMTAs as PMTA bundles. We have received 12 PMTA bundles so far, and a bundle may include PMTAs for one product or for hundreds of products. The largest bundle we have received so far included 287 different products.

c. Original and Supplemental PMTAs

The proposed rule, if finalized, codifies the requirements for supplemental PMTAs to allow firms to cross reference studies in PMTAs that we have previously reviewed and issued a marketing order, thus reducing the costs of subsequent PMTAs for related products. The final regulatory impact analysis for the Deeming Rule (Ref. 4) accounted for the costs of the supplemental PMTAs and assumed that firms would submit supplemental PMTAs after the Deeming compliance period. In this baseline analysis, we use the same assumptions that firms

[12] We use Dun and Bradstreet's small business indicator variable to determine whether a firm is a small business.

would submit original PMTAs during the Deeming compliance period and submit supplemental PMTAs after the Deeming compliance period. We request comment on these assumptions.

d. Follow-On Submissions

Firms may submit follow-on PMTA bundles for any products that do not receive a marketing order. We assume that firms would only submit follow-on submissions for bundles that we have refused to accept or refused to file in a previous review.[13]

6. Baseline Costs for PMTA Submission and Review

In this section, we estimate the updated costs to submit and review PMTAs for deemed products in the post-Deeming baseline. We make the following updates to the estimates in the regulatory impact analysis for the Deeming rule:

- We updated cost estimates to account for wage growth and inflation, using the data in Table 5 and Table 6.
- We accounted for changes in the compliance date for deemed products.
- We adjust the estimates to account for inefficiencies in the submission and review of PMTAs by modeling incomplete or partially complete submissions and follow-on submissions.
- We account for market consolidation that has occurred since the publication of the Deeming Final Rule by modeling firms' decision to submit PMTA bundles.

In the absence of this proposed rule, firms have limited information about the content and format requirements for PMTAs. For example, as of 2017, we received 12 bundles, of which we accepted 5 bundles and filed 3 bundles. Moreover, in 2016 we refused to accept about 365 PMTAs received from manufacturers of deemed tobacco products because these applications lacked the basic information to allow us to conduct the filing review shown in Figure 1[14]. Such limited experience creates uncertainty about the effort needed to submit and review PMTA bundles through all three review stages. Therefore, we use a Monte Carlo simulation model to estimate the total baseline costs for PMTAs. A Monte Carlo simulation is a way to incorporate uncertainty into a benefit-cost analysis.[15] In this section, we describe the key assumptions we make in our model. We request comment on our assumptions.

[13] Through this assumption, we exclude the possibility of abbreviated "resubmissions" for products with no marketing orders. However, to incorporate resubmissions for products with no marketing orders into our analysis, we would need to predict the probability that a bundle receives a no marketing order. As explained in section b on marketing orders, we cannot predict this probability.

[14] On August 8, 2016, we published a direct final rule (and a companion proposed rule), Refuse To Accept Procedures for Premarket Tobacco Product Submissions (RTA), which specified the basic information we required to conduct our acceptance review. We received comments on the direct final rule and subsequently published the final rule on December 29, 2016. Because we have received so few PMTAs since the RTA final rule, we assume that the RTA rule did not completely eliminate uncertainty about our expectations for the information we want submitted in a PMTA, creating a disincentive for manufacturers of deemed tobacco products to submit PMTAs before the end of the Deeming compliance period.

[15] Palisade offers a succinct description of Monte Carlo simulations at https://www.palisade.com/risk/monte_carlo_simulation.asp. We run 10,000 iterations of our model, using an initial seed of 1.

a. Completeness of PMTA Bundles

In our model, we define the "completeness" of a PMTA bundle based on the results of the three stages of review shown in Figure 1. We label PMTA bundles that stop at the acceptance review stage as "incomplete"; we label PMTA bundles that stop at the filing review stage as "partially complete". We label all PMTA bundles that finish substantive review as "complete". Complete bundles include bundles with marketing orders, bundles with no marketing orders, and bundles that firms withdraw during substantive review. Having gone through the initial stages of our review process, we expect that firms will better understand our expectations for the content and format of PMTAs. Thus, in our analysis we assume that firms submit complete follow-on bundles for all incomplete or partial complete initial bundles.

Based on the 12 bundles we have received thus far, we assume that initial bundles would be 58 percent incomplete, 17 percent partially complete, and 25 percent complete (Table 7).

Table 7. Baseline Completeness of Initial PMTA Bundle Submissions

Completeness	Number of Bundles to Date	Percent of Bundles
Incomplete	7	58%
Partially Complete	2	17%
Complete	3	25%

b. Marketing Orders

We only grant marketing orders through the PMTA pathway to products that we determine are appropriate for the protection of public health based on scientific review of the contents of the application. The probability that a bundle will receive a marketing order depends on many factors that we can't observe or predict, given our limited experience reviewing PMTAs. For simplicity, we assume that our substantive review would find that all products in complete bundles are appropriate for the protection of public health and would receive marketing orders. Therefore, our analysis estimates the upper bound number of marketing orders.

c. Number of PMTA Bundles

We assume that firms would only submit PMTAs when the net expected profits from submission are positive. We expect that firms decide whether to submit a PMTA bundle by comparing the discounted expected profits over the products' lifetime[16] to the discounted expected cost of the PMTA bundle submission. We describe our methods to estimate the number of submitted bundles, based on this assumption, in detail in Section V. We request comment on the assumptions used to estimate the expected number of submitted bundles.

An alternative data source to estimate the number of PMTA submissions is our Tobacco Registration and Listing (TRLM) data. This data includes all tobacco products listed with FDA. Because the cost of listing a product with us is relatively low, we expect that this data would

[16] In our simulation, we assume that a bundle's profitable life is a uniform random variable between 5 and 20 years. We find that our results are relatively insensitive to assumptions about the length of profitable life.

inflate our estimate of PMTA bundles. Notably, we require manufacturers to submit a list of all ingredients in each marketed tobacco product.[17] Even though the cost of submitting an ingredients list is only slightly higher than the cost of listing a product with us, we find that the number of ENDS products with ingredient listings is much lower than the number of listed ENDS products. Thus, we use actual market data to estimate the expected number of submitted bundles because it can capture firm decisions better than the listing data.

Whether the discounted expected profits over the product lifetime exceed the discounted costs of a PMTA submission for a given bundles depends on 1) when we issue a marketing order for the bundle, 2) the expected annual profits from marketing the bundles under that marketing order, and 3) the expected cost of submitting the PMTA bundle. We use the time of initial submission and the time of follow-on submission of the bundle to discount the expected cost of the PMTA submission. We discount annual profits based on the time when we expect to issue a marketing order. We model these inputs using data on PMTA submission costs and bundle completeness, discussed in this analysis, as well as analysis informed, in part, by Nielsen Retail Measurement Services (RMS) data.[18]

We adopt this approach to allow the number of submitted bundles to vary as the efficiency of PMTA submission and review improves with the rule. In Table 8, we show the baseline number of e-liquid PMTA bundles we expect firms would submit annually, by completeness. These estimates include follow-on bundles, which we believe can take firms a few weeks to a few years to assemble for submission. On average, we assume that firms would submit between 1 and 3 years after the initial submission.[19]

Table 8. Number of E-Liquid Bundles Submitted in the Baseline

Year	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total[a]
2019	0.00	0.00	0.00	0.00	0.00	0.00
2020	7.40	4.93	17.27	0.00	0.00	29.61
2021	1.55	1.03	3.61	1.63	5.71	13.52
2022	1.54	1.03	3.60	1.99	6.97	15.13
2023	1.54	1.03	3.60	2.33	8.17	16.67
2024 and On	1.56	1.04	3.63	1.04	3.62	10.89

[17] As discussed in guidance, available at https://www.fda.gov/media/101162/download.

[18] FDA's own analyses and calculations are informed, in part, on data reported by The Nielsen Company through its RMS service for the electronic vapor and smokeless product categories for the 32-week period beginning December 31, 2017 and ending August 11, 2018 for the total United States market and Convenience Stores and Expanded All Outlets Combined (xAOC) channels. The conclusions informed by the Nielsen data are those of the FDA and do not reflect the views of Nielsen. Nielsen is not responsible for and had no role in and was not involved in analyzing and preparing the results reported herein, or in developing, reviewing or confirming the research approaches or methodologies used in connection with this report, including without limitation, the bundle compositions. All references to Nielsen in this document refer to the data described above and are subject to the above disclaimer.

[19] In our simulation, the time to follow-on submission is a uniform random integer between 1 year and 3 years.

[a] Mean values from simulation.

In Table 9, we estimate the baseline number of e-cigarette PMTA bundles submitted annually, by completeness, including follow-on bundles.

Table 9. Number of E-Cigarette Bundles Submitted in the Baseline

Year	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total[a]
2019	0.00	0.00	0.00	0.00	0.00	0.00
2020	4.87	3.25	11.36	0.00	0.00	19.47
2021	0.60	0.40	1.39	1.07	3.75	7.21
2022	0.59	0.40	1.38	1.22	4.26	7.85
2023	0.59	0.40	1.38	1.35	4.73	8.45
2024 and On	0.60	0.40	1.39	0.40	1.38	4.16

[a] Mean values from simulation.

From Table 8 and Table 9, we observe that we would receive many incomplete and partially complete PMTAs at the end of the Deeming compliance period. Specifically, we estimate that we would receive between 7 and 28 incomplete bundles and between 2 and 14 partially complete bundles in 2020. These bundles could represent approximately 293 total PMTAs, each requiring us to divert resources from substantive review of complete applications.

d. Baseline Cost to Prepare and Submit a PMTA Bundle

We assume that complete PMTA bundles would meet the format and content requirements reaching substantive review described in this proposed rule. The costs to prepare a PMTA bundle include:

- Administrative staff time
- Composition, design, and manufacturing studies
- Toxicological studies
- Human studies
- Environment assessments

To estimate the baseline cost of e-liquid and e-cigarette PMTA bundles, we use information from the final regulatory impact analysis for the Deeming Rule (Ref. 4). In that analysis, the costs to prepare a PMTA for a deemed tobacco product accounted for the costs to comply with the format and content requirements of a PMTA as described in the TCA. To avoid double counting costs and cost savings, we assume that the analysis for the Deeming Rule accounted for the costs to comply with most of the format and content requirements for a complete PMTA described in this proposed rule. As stated previously, we update the PMTA

costs for deemed tobacco products to account for unanticipated inefficiencies in the PMTA pathway excluded from the final regulatory impact analysis for the Deeming Rule.

Based on these assumptions, we use the cost estimates from the Deeming Rule as our estimate of the total administrative costs and studies costs for complete ENDS PMTA bundles. We update these cost estimates to account for inflation in Table 10. We use GDP price indices from the Bureau of Economic Analysis from Table 6 to inflate costs to 2017 dollars and use 2017 wages from Table 5 to value the time of administrative and scientific staff.

The cost to prepare and submit a PMTA bundle depends on the number of products in each bundle. Specifically, the costs of administrative staff time, composition, design, and manufacturing studies, and environmental assessments all increase as the number of products per bundle increase. Using Nielsen RMS data, in part (see Footnote 18), we estimate that e-liquid bundles contain, on average, 8.7 products per bundle and that e-cigarette bundles contain, on average, 4.2 products per bundle. However, some bundles submitted for e-liquids have contained hundreds of products per bundle. Therefore, the estimates in Table 10 may underestimate the cost to prepare and submit an e-liquid bundle by underestimating the number of products per bundle. We request comment on these estimates.

Table 10. Updated Deeming Estimates of Baseline Costs to Prepare and Submit a PMTA Bundle

Product Type	Type of PMTA	Administrative Cost	Studies Cost	Total Cost
E-Liquid	Original	$17,588	$1,299,174	$1,316,762
	Supplemental	$16,898	$1,188,842	$1,205,740
E-Cigarette	Original	$10,456	$1,640,953	$1,651,409
	Supplemental	$8,855	$897,241	$906,096

The cost of preparing and submitting a PMTA bundle depends on the completeness of the bundle. Incomplete and partially complete bundles do not meet the format and content requirements for a PMTA to reach substantive review. Meeting these format and content requirements has a cost; therefore, incomplete and partially complete bundles cost less than complete bundles. For partially complete initial bundles, we assume that firms incur 100 percent of the administrative cost but only 67 percent of the studies cost. For incomplete initial bundles, we assume that firms incur 100 percent of the administrative cost but only 33 percent of the studies cost.

The cost of preparing and submitting a PMTA bundle also depends on whether the bundle is an initial submission or a follow-on submission. Because we assume that all follow-on submissions are complete, firms must incur the additional cost to make an incomplete or partially complete bundle "complete". For follow-on bundles that followed partially complete submissions, we assume that firms again incur 100 percent of the administrative cost and the remaining 33 percent of the studies cost. For follow-on bundles that followed incomplete submissions, we assume that firms again incur 100 percent of the administrative cost and the remaining 67 percent of the studies cost.

Given these assumptions and the assumption that firms would submit original PMTAs during the DCP and supplemental PMTAs in the post-DCP, we summarize the unit cost to prepare and submit a PMTA bundle by bundle type in Table 11.

Table 11. Baseline Unit Cost to Prepare and Submit a PMTA Bundle, by Bundle Type

Product Type	Period	Complete Initial Bundles	Partially Complete Initial Bundles	Incomplete Initial Bundles	Complete Follow-On Bundles that were Initially Partially Complete	Complete Follow-On Bundles that were Initially Incomplete
E-Liquid	DCP	$1,316,762	$883,704	$450,646	$450,646	$883,704
	Post-DCP	$1,205,740	$809,460	$413,179	$413,179	$809,460
E-Cigarette	DCP	$1,651,409	$1,104,425	$557,440	$557,440	$1,104,425
	Post-DCP	$906,096	$607,016	$307,935	$307,935	$607,016

To estimate the total baseline cost of preparing and submitting PMTA bundles, we multiply the unit cost in Table 11 by the number of bundles in Table 8 and Table 9, then discount over 20 years. In Table 12, we present our estimate the total cost to prepare and submit PMTA bundles over 20 years. The annualized baseline costs equal $11.90 million at a 3 percent discount rate and $12.43 million at a 7 percent discount rate.

Table 12. Total Baseline Cost to Prepare and Submit PMTA Bundles over 20 Years ($ m)

Value	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total Cost[a]
Present Value (3%)	$49.40	$22.09	$39.35	$9.09	$62.44	$182.36
Present Value (7%)	$39.24	$17.54	$31.25	$6.72	$46.16	$140.92
Annualized Value (3%)	$3.22	$1.44	$2.57	$0.59	$4.07	$11.90
Annualized Value (7%)	$3.46	$1.55	$2.76	$0.59	$4.07	$12.43

[a] Mean values from simulation.

e. Baseline Cost of Reviewing a PMTA Bundle

Though we codify many of our review procedures in this proposed rule, we currently conduct acceptance, filing, and substantive reviews for PMTAs. We therefore include the cost for each level of review in our baseline. In Table 13, we estimate the cost of each stage of review per bundle, based on labor hour estimates from CTP's Office of Science, and the fully loaded wage for CTP staff from Table 5.

Table 13. Baseline Cost to Review a PMTA Bundle per Stage of Review

Product Type[20]	Period	Cost per Acceptance Review	Cost per Filing Review	Cost per Substantive Review	Total Cost
E-Liquid	DCP	$485	$13,817	$623,621	$637,922
	Post-DCP	$469	$12,814	$584,163	$597,446
E-Cigarette	DCP	$575	$18,164	$801,354	$820,093
	Post-DCP	$499	$14,460	$650,359	$665,318

In Table 14, we estimate the unit cost to review a PMTA bundle, by bundle type.

Table 14. Baseline Cost to Review a PMTA Bundle, by Bundle Type

Product Type	Period	Complete Initial or Follow-on Bundles[a]	Partially Complete Initial Bundles[b]	Incomplete Initial Bundles[c]
E-Liquid	DCP	$637,922	$14,301	$485
	Post-DCP	$597,446	$13,283	$469
E-Cigarette	DCP	$820,093	$18,739	$575
	Post-DCP	$665,318	$14,959	$499

[a] Includes the costs of all three stages of review.
[b] Includes the costs of acceptance and filing review.
[c] Includes the cost of acceptance review.

To estimate the total baseline cost of reviewing PMTA bundles, we multiply the unit cost in Table 14 by the number of bundles in Table 8 and Table 9, then discount over 20 years. In Table 15, we estimate the total cost to review PMTA bundles over 20 years. The annualized baseline costs equal $6.08 million at a 3 percent discount rate and $6.20 million at a 7 percent discount rate.

Table 15. Total Baseline Cost to Review PMTA Bundles over 20 Years ($m)

Value	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total Cost[a]
Present Value (3%)	$26.10	$0.39	$0.05	$14.80	$51.81	$93.15

[20] The costs per stage of review are higher for e-liquid PMTA bundles than for e-cigarette PMTA bundles. From the regulatory impact analysis for the Deeming Rule (Ref. 4), e-liquid PMTA bundles are, on average, more complex than e-cigarette PMTA bundles. Complex PMTA bundles are costlier to review than less complex PMTA bundles.

Similarly, the costs per stage of review are higher also during the Deeming compliance period than they are after the Deeming compliance period. We expect that original PMTAs are, on average, more complex than supplemental PMTAs. Because we assume that firms submit original PMTAs during the DCP and supplemental PMTAs in the post-DCP, PMTAs submitted during the DCP are costlier to review than PMTAs submitting in the post-DCP.

Present Value (7%)	$20.56	$0.31	$0.04	$10.98	$38.42	$70.30
Annualized Value (3%)	$1.70	$0.03	$0.00	$0.97	$3.38	$6.08
Annualized Value (7%)	$1.81	$0.03	$0.00	$0.97	$3.39	$6.20

[a] Mean values from simulation.

f. Cost of Deficiency Letters

During review, we may issue deficiency letters requesting amendments to a PMTA. Generally, we issue these letters during substantive review. In our limited history reviewing PMTAs, on average we have issued 4 deficiency letters per bundle during substantive review. CTP's Office of Science estimates that it takes us between 71 hours and 266 hours to prepare each letter.[21]

Firms would prepare amendments to PMTA bundles in response to deficiency letters. These amendments contain additional information that we need to complete substantive review. Therefore, we assume that the total cost to prepare a complete PMTA bundle (from Table 12) includes the cost for industry to prepare amendments in response to deficiency letters.

In Table 16, we estimate the cost per deficiency letter to FDA using the wage for CTP staff from Table 5.

Table 16. Baseline per Bundle Costs of Deficiency Letters to FDA ($)[a,b]

Cost per Letter	$20,080
Average Number Letters	4
Total Cost per Complete Bundle	$80,319

[a] We assume that we only issue deficiency letters for complete bundles.
[b] Mean values from simulation.

To estimate the total baseline cost of issuing deficiency letters for complete PMTA bundles, we multiply the unit cost in Table 16 by the number of complete initial and follow-on bundles from Table 8 and Table 9, then discount over 20 years. In Table 17, we estimate the total cost to issue deficiency letters for PMTA bundles over 20 years. The annualized baseline costs equal $0.77 million at a 3 percent discount rate and $0.78 million at a 7 percent discount rate.

Table 17. Total Baseline Cost to Issue Deficiency Letters over 20 Years ($m)[a]

Present Value (3%)	$11.83
Present Value (7%)	$8.90
Annualized Value (3%)	$0.77
Annualized Value (7%)	$0.78

[a] Mean values from simulation.

g. Cost of Processing Unnecessary Data

Before we begin acceptance review for a PMTA bundle, we must electronically process all the submission materials. With our limited experience reviewing PMTAs we have found that firms often submit large amounts of raw data, which we do not require for our review. We assume that the number of hours we spend processing unnecessary data in the baseline is a uniform random variable between 40 hours and 80 hours. We also assume that we incur these costs before beginning acceptance review.[22] Using the wage from CTP staff from Table 5, we estimate the mean cost to process unnecessary data is $7,158 per bundle.

We assume that firms do not submit unnecessary data for follow-on bundles. Given this assumption, we multiply the unit cost to process unnecessary data by the total number of initial bundles from Table 8 and Table 9. In Table 18, we estimate the total baseline cost to process unnecessary data over 20 years. The annualized baseline costs equal $0.08 million at a 3 percent discount rate and at a 7 percent discount rate.

Table 18. Total Baseline Cost to Process Unnecessary Data over 20 years ($m)[a]

Present Value (3%)	$1.16
Present Value (7%)	$0.90
Annualized Value (3%)	$0.08
Annualized Value (7%)	$0.08

[a] Mean values from simulation.

h. Total Baseline Costs of PMTA Submission and Review

We present the simulated estimates of the present value and annualized value of baseline costs of PMTA submission and review costs over 20 years in Table 19. The mean annualized cost equals $18.83 million at a 3 percent rate, with a 90 percent confidence interval ranging from $17.22 million to $20.39 million. The mean annualized cost equals $19.50 million at a 7 percent rate, with a 90 percent confidence interval ranging from $17.60 million to $21.35 million.

Table 19. Total Baseline Costs of PMTA Submission and Review over 20 Years ($m)[a]

Value	5th Percentile	Mean[b]	95th Percentile
Present Value (3%)	$263.82	$288.50	$312.50
Present Value (7%)	$199.54	$221.02	$242.05
Annualized Value (3%)	$17.22	$18.83	$20.39
Annualized Value (7%)	$17.60	$19.50	$21.35

[a] Baseline cost estimates represent the modified Deeming costs for ENDS products.
[b] Only mean values sum in simulation results.

The estimate in Table 19 represent the total baseline costs for firms to submit PMTA bundles and for us to review these bundles in the absence of rulemaking. In the next section, we

[22] In our simulation, we assume that the number of labor hours required to process unnecessary data in the baseline is a uniform random variable between 40 hours and 80 hours.

estimate these total costs with rulemaking. The impact of this rulemaking is the incremental difference between the total costs with rulemaking and the total costs without rulemaking.

E. Benefits of the Proposed Rule

1. Direct Impacts of the Proposed Rule on PMTA Submission and Review

In this section, we discuss how we incorporate the impacts of the proposed rule into our model, as described in the Baseline section. We estimate the total costs of submitting PMTAs with rulemaking. The impact of this rulemaking equals the net change in the total costs of submitting PMTAs.

a. PMTA Bundle Completeness

As illustrated in Table 7, most of the PMTA bundles that we have received to date have been incomplete. Of the 12 bundles that we have received thus far, we have refused to accept 7 bundles, or 58 percent. We expect that we would receive more complete bundles if firms had more detailed information about the format and content requirements of a PMTA. This proposed rule, if finalized, would communicate our expectations to industry. Because firms have incentives to submit complete bundles, we expect that communicating our expectations to industry would increase the completeness of submitted bundles.

To estimate the impact of the proposed rule on the completeness of PMTA bundles, we use data from our review of Premarket Applications (PMAs) for medical devices. Like CTP's review of PMTAs, the Center for Devices and Radiological Health's review of PMAs includes an acceptance review, a filing review, and a substantive review. However, unlike premarket review of tobacco products, we have conducted premarket review of medical devices for many years.[23] We collected data on the number of PMAs by completeness (Ref. 8). As shown in Table 20, we receive more complete PMAs for medical devices than the PMTAs we receive for tobacco products.

Table 20. Completeness of PMAs for Medical Devices from 2013 to 2017

Application Completeness	Number of PMAs	Percent of PMAs
Complete	180	83%
Partially Complete	9	4%
Incomplete	27	13%

Industry experience with premarket applications may explain some of the difference in the completeness of medical device applications and tobacco product applications. To capture uncertainty in the impact of the proposed rule on completeness, we consider a range of possible outcomes using probability distributions. In the lower bound, the completeness of PMTA bundles is the same as the completeness of the bundles we have received to date from Table 7.

[23] The Medical Device Amendments of 1976 to the FD&C Act established premarket review of medical devices.

In the upper bound, the completeness of PMTA bundles is the same as the completeness of the medical device PMAs we received from 2013 to 2017.[24]

b. Administrative Cost per Bundle

The proposed rule includes some new requirements for PMTAs. For example, firms would submit any marketing plans they have already developed by the time of PMTA submission, or state that they have no marketing plans. To account for the incremental burden of this rulemaking, we assume that the administrative cost per bundle would increase by between 10 and 20 percent. We request comment on this assumption.

In Table 21, we estimate the costs to prepare and submit a complete PMTA bundle with rulemaking. The administrative cost would increase by, on average, 15 percent but the studies cost would not change.

Table 21. Costs to Prepare and Submit a Complete PMTA Bundle with Rulemaking

Product Type	Type of PMTA	Administrative Cost[a]	Studies Cost	Total Cost[a]
E-Liquid	Original	$20,227	$1,299,174	$1,319,400
	Supplemental	$19,433	$1,188,842	$1,208,275
E-Cigarette	Original	$12,025	$1,640,953	$1,652,977
	Supplemental	$10,183	$897,241	$907,425

[a] Mean value from simulation.

c. Cost per Review

If finalized, we expect that the proposed format and content requirements for PMTAs would encourage firms to submit better organized and more complete PMTAs making our review more efficient. As compared to the baseline costs per review stage (Table 13), CTP's Office of Science expects that the cost per acceptance review would rise slightly because the proposed rule includes some new acceptance requirements. We expect that the cost per filing review and the cost per substantive review would fall as firms submit PMTAs that better meet the content and format requirements for PMTAs. In Table 22, we show our estimate of the costs for each stage of review.

Table 22. Estimated Cost to Review a PMTA Bundle per Stage of Review with Rulemaking

Product Type	Period	Cost per Acceptance Review	Cost per Filing Review	Cost per Substantive Review

[24] Specifically, we use two random variables to estimate the completeness of bundles under the proposed rule. The first random variable is the probability that we accept a bundle, which we assume has a uniform distribution. From Table 7, the lower bound is the percent of bundles to date that were complete or partially complete (42 percent). From Table 20, the upper bound is the percent of PMAs from 2013 to 2017 that were partially complete or complete (88 percent).
The second random variable is the probability that we file a bundle, conditional on having accepted the bundle. We also assume that this random variable has a uniform distribution. From Table 7, the lower bound number of bundles to date that were complete, divided by the number of bundles to date that were complete or partially complete (60 percent). From Table 20, the upper bound is the number of PMAs from 2013 to 2017 that were complete divided by the number of PMAs that were partially complete or complete (95 percent).

E-Liquid	DCP	$627	$6,908	$501,124
	Post-DCP	$600	$6,407	$470,845
E-Cigarette	DCP	$756	$9,082	$642,316
	Post-DCP	$647	$7,230	$522,671

d. Deficiency Letters

We would expect to issue fewer deficiency letters during substantive review under the proposed rule compared to the number in the baseline. CTP's Office of Science estimates that we would issue between 1 and 2 deficiency letters per bundle under the proposed rule. Although the number of deficiency letters issued per bundle would change, we assume that our cost to prepare a deficiency letter would remain unchanged.

e. Unnecessary Data Costs

The proposed rule, if finalized, includes detailed format requirements and specifically outlines the types of data that we need submitted in a PMTA. For example, the preamble to the proposed rule discusses the detailed format requirements for PMTAs[25], including the requirement that applicants submit line data instead of "raw" data as it allows for a more efficient review process. Given the format requirements and the detailed information provided to applicants in the rule, we assume that firms would no longer submit unnecessary data.

f. Number of ENDS PMTA Bundles

We would expect to receive fewer incomplete bundles, partially complete bundles, and follow-on bundles, and we would expect to receive more complete initial bundles. In Table 23, we estimate the number of e-liquid PMTA bundles submitted annually under the proposed rule, if finalized.

Table 23. Estimated Number of E-Liquid Bundles Submitted with Rulemaking

Year	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total[a]
2019	0.00	0.00	0.00	0.00	0.00	0.00
2020	14.89	4.33	10.50	0.00	0.00	29.73
2021	3.11	0.90	2.20	1.42	3.47	11.09
2022	3.10	0.91	2.19	1.73	4.26	12.19
2023	3.10	0.90	2.19	2.07	4.95	13.21
2024 and On	3.13	0.91	2.21	0.91	2.20	9.37

[a] Mean values from simulation.

[25] Proposed § 1114.7(k)(3).

In Table 24, we estimate the number of e-cigarette PMTA bundles we expect firms would submit annually with rulemaking. We would expect to receive fewer incomplete bundles, partially complete bundles, and follow-on bundles, and we would expect to receive more complete initial bundles.

Table 24. Estimated Number of E-Cigarette Bundles Submitted with Rulemaking

Year	Complete Initial Bundles[a]	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total[a]
2019	0.00	0.00	0.00	0.00	0.00	0.00
2020	9.80	2.85	6.91	0.00	0.00	19.56
2021	1.20	0.35	0.85	0.93	2.28	5.60
2022	1.20	0.35	0.84	1.06	2.61	6.05
2023	1.19	0.35	0.84	1.20	2.86	6.45
2024 and On	1.20	0.35	0.85	0.35	0.84	3.58

[a] Mean values from simulation.

We find that rulemaking would slightly change the total number of submitted bundles as well as the type of submitted bundles. For example, we estimate that firms would submit fewer total bundles in 2022 with rulemaking than without rulemaking, due to a reduction in the number of follow-on submissions.

i. Total Cost of PMTA Submission and Review for ENDS with Rulemaking

We present the simulated estimates of the present value and annualized value of costs of PMTA submission and review costs for ENDS over 20 years with rulemaking in Table 25. The mean annualized cost equals $17.71 million at a 3 percent rate, with a 90 percent confidence interval ranging from $16.35 million to $19.02 million. The mean annualized cost equals $18.59 million at a 7 percent rate, with a 90 percent confidence interval ranging from $16.97 million to $20.10 million.

Table 25. Total Costs of ENDS PMTA Submission and Review over 20 Years with Rulemaking ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	$250.57	$271.35	$291.42
Present Value (7%)	$192.37	$210.69	$227.89
Annualized Value (3%)	$16.35	$17.71	$19.02
Annualized Value (7%)	$16.97	$18.59	$20.10

[a] Only mean values sum in simulation results.

The impact of this rulemaking on the costs to submit and review PMTAs for ENDS is the difference between the total costs with rulemaking (Table 25) and the total costs without rulemaking (Table 19). We estimate this difference in Table 26 below. The change in the mean annualized cost equals -$1.12 million at a 3 percent rate, with a 90 percent confidence interval ranging from -$1.83 million to -$0.17 million. The change in the mean annualized cost equals -$0.91 million at a 7 percent rate, with a 90 percent confidence interval ranging from -$1.82 million to $0.30 million.

Table 26. Change in Total Costs of ENDS PMTA Submission and Review over 20 Years from Rulemaking ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	($28.10)	($17.15)	($2.60)
Present Value (7%)	($20.60)	($10.33)	$3.44
Annualized Value (3%)	($1.83)	($1.12)	($0.17)
Annualized Value (7%)	($1.82)	($0.91)	$0.30

[a] Only mean values sum in simulation results.

However, in this analysis, we break down the incremental impact of rulemaking to submit and review ENDS PMTAs into costs savings and costs. In Table 27, we summarize these impacts. Firms would experience cost savings by submitting fewer incomplete, partially complete, and follow-on bundles. However, firms would incur costs by submitting more initially complete bundles. Firms would also incur higher administrative costs for all PMTA bundles.

Similarly, we show the net impact of rulemaking on the cost to FDA to review PMTAs. We would receive fewer incomplete, partially complete, and follow-on bundles, creating cost savings. We would also experience cost savings as the cost per filing review and the cost per substantive review falls. However, we would incur costs to review more complete bundles, and costs related to the increase in the cost per acceptance review.

Table 27. Impact of Rulemaking on Costs of ENDS PMTA Submission and Review

Impacted Cost	Cost Savings	Costs
Industry Cost of PMTA Submission	Fewer incomplete, partially complete, and follow-on submissions	(1) More complete submissions (2) Higher administrative cost per bundle
FDA Cost of PMTA Review	(1) Fewer incomplete, partially complete, and follow-on reviews (2) Lower cost per filing and substantive review	(1) More complete reviews (2) Higher cost per acceptance review
FDA Cost for Deficiency Letters	Fewer deficiency letters	None
FDA Cost of Unnecessary Data	No processing of unnecessary data	None

g. Premarket Review for Originally Regulated Products

Though this rule does not implement the PMTA requirements for originally regulated tobacco product categories, this proposed rule is our first rulemaking regarding the requirements established by the TCA. For the purposes of this analysis, we assume a pre-statutory baseline for originally regulated tobacco product categories. Such new tobacco products could include innovative modifications of originally regulated products.

To date, we have received a few PMTA bundles for originally regulated products. In general, these PMTA bundles have been for smokeless tobacco products. Therefore, throughout our analysis, we use the market for smokeless tobacco products to characterize the market for originally regulated products that would use the PMTA pathway. We request comment on this assumption.

2. Cost Savings to Firms from ENDS PMTA Preparation and Submission

The proposed rule, if finalized, would increase the unit costs to prepare and submit an ENDS PMTA bundle (from Table 21), but would reduce the number of partially complete initial bundles, the number of incomplete initial bundles, and the number of follow-on bundles, generating cost-savings to firms. We estimate that the total costs to prepare partially complete, incomplete, and follow-on bundles would fall due to this rulemaking, creating net cost savings. In Table 28, we show our estimate of the total cost-savings to firms from PMTA preparation and submission over 20 years. We estimate that the proposed rule would generate $2.85 million in annualized cost savings to firms at a 3 percent discount rate and $2.94 million in annualized cost savings to firms at a 7 percent discount rate.

Table 28. Total Cost Savings to Firms from ENDS PMTA Preparation and Submission ($m)

Value	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total Cost Savings[a]
Present Value (3%)	$2.70	$15.41	$1.12	$24.45	$43.67
Present Value (7%)	$2.14	$12.24	$0.83	$18.08	$33.28
Annualized Value (3%)	$0.18	$1.01	$0.07	$1.60	$2.85
Annualized Value (7%)	$0.19	$1.08	$0.07	$1.59	$2.94

[a] Mean values from simulation.

3. Cost Savings to FDA from ENDS PMTA Review

Because the proposed rule, if finalized, would change the unit cost of acceptance review, filing review, and substantive review, the unit cost to review a PMTA bundle would change. In Table 29, we show our estimate of the unit cost to review a PMTA bundle, by bundle type.

Table 29. Cost to Review an ENDS PMTA Bundle with Rulemaking, by Bundle Type

Product Type	Period	Complete Initial or Follow-on Bundles	Partially Complete Initial Bundles	Incomplete Initial Bundles
E-Liquid	DCP	$508,660	$7,535	$627
	Post-DCP	$477,852	$7,007	$600
E-Cigarette	DCP	$652,154	$9,838	$756
	Post-DCP	$530,548	$7,877	$647

The proposed rule, if finalized, would reduce the number of partially complete initial bundles, the number of incomplete initial bundles, and the number of follow-on bundles. As a result, the proposed rule would generate some cost savings for FDA. In Table 28, we show our estimate of the total cost savings for PMTA review over 20 years. We estimate that the proposed rule would generate $2.04 million in annualized cost savings at a 3 percent discount rate and $2.05 million in annualized cost savings at a 7 percent discount rate.

Table 30. Total Cost Savings to FDA from ENDS PMTA Review ($m)

Value	Partially Complete Initial Bundles[a]	Incomplete Initial Bundles[a]	Complete Follow-On Bundles that were Initially Partially Complete[a]	Complete Follow-On Bundles that were Initially Incomplete[a]	Total Cost Savings[a]
Present Value (3%)	$0.21	$0.01	$4.43	$26.62	$31.27
Present Value (7%)	$0.17	$0.01	$3.28	$19.74	$23.20
Annualized Value (3%)	$0.01	$0.00	$0.29	$1.74	$2.04
Annualized Value (7%)	$0.01	$0.00	$0.29	$1.74	$2.05

[a] Mean values from simulation.

4. Cost Savings from Deficiency Letters for ENDS

The net effect of the proposed rule, if finalized, on the effort required to issue and respond to deficiency letters for ENDS products could be positive or negative. The number of deficiency letters per complete bundle would fall under the proposed rule, but we would issue more deficiency letters for more bundles because we would expect to receive more complete initial bundles with rulemaking. However, we expect that overall rulemaking would generate net cost savings from fewer deficiency letters. In Table 31, we show our estimate of the total cost savings from fewer deficiency letters over 20 years. We estimate that the proposed rule would

generate $0.47 million in annualized cost savings at a 3 percent discount rate and $0.48 million in annualized cost savings at a 7 percent discount rate.

Table 31. Total Cost Savings to FDA from Fewer Deficiency Letters for ENDS ($m)

Present Value (3%)	$7.24
Present Value (7%)	$5.40
Annualized Value (3%)	$0.47
Annualized Value (7%)	$0.48

[a] Mean values from simulation.

5. Cost Savings from Unnecessary Data

In Table 18, we estimated the total baseline cost to process unnecessary data. Under the proposed rule, if finalized, we would no longer receive unnecessary data. Therefore, we expect that the proposed rule would generate cost-savings for FDA by avoiding the cost to process unnecessary data. Based on the estimates in Table 18, the annualized cost savings to FDA would equal $0.08 million at a 3 percent discount rate and a 7 percent discount rate.

6. Total Cost Savings from the Proposed Rule

In Table 32, we present our estimate of the total cost savings from the proposed rule over 20 years. The mean annualized cost savings equal $5.44 million at a 3 percent rate, with a 90 percent confidence interval ranging from $2.54 million to $9.03 million. The mean annualized cost savings equal $5.54 million at a 7 percent rate, with a 90 percent confidence interval ranging from $2.57 million to $9.23 million.

Table 32. Total Cost Savings from the Proposed Rule over 20 Years ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	$38.86	$83.34	$138.43
Present Value (7%)	$29.10	$62.79	$104.59
Annualized Value (3%)	$2.54	$5.44	$9.03
Annualized Value (7%)	$2.57	$5.54	$9.23

[a] Only mean values sum in simulation results.

F. Costs of the Proposed Rule

1. One-Time Cost to Read and Understand the Rule

We expect that all potential PMTA applicants would incur costs to read and understand the proposed rule at the time of publication of a final rule. The proposed rule has approximately 85,000 words. Consistent with Guidelines from the Department of Health and Human Services (Ref. 5), we assume that the reading speed of regulation reviewers follows a normal distribution with a mean of 228 words per minute and a standard deviation of 30 words per minutes (Ref. 9). Because the proposed rule is complex, we expect that 2 lawyers would spend time to read and understand the proposed rule for each small firm, and 4 lawyers would spend time to read and understand the proposed rule for each large firm.

We expect that manufacturers would spend time to read and understand the rule to make informed choices about their options after the Deeming compliance period. Although we expect that most vape stores and specialty tobacco product manufacturers would learn about the rule from industry associations, rather than paying a lawyer to read the rule, we lack information to predict the exact number of firms that would incur these costs. To account for uncertainty in the number of firms that would read and understand the rule, we use the total number of affected firms (2,450) as the upper bound number of firms. For the lower bound, we subtract the number of firms that only own vape shops from the total number of affected firms (2,450 – 750 = 1,400).[26]

Using the mean wage for lawyers from Table 5, in Table 33 we estimate the annualized costs over 20 years would equal $0.25 million at a 3 percent discount rate and $0.34 million at a 7 percent discount rate.

Table 33. Total One-Time Cost to Read and Understand the Proposed Rule ($m)[a]

Present Value (3%)	$3.90
Present Value (7%)	$3.90
Annualized Value (3%)	$0.25
Annualized Value (7%)	$0.34

[a] Mean values from simulation.

2. Costs to Firms from ENDS PMTA Preparation and Submission

The proposed rule, if finalized, would increase the unit costs of preparing and submitting a PMTA bundle (from Table 21) and increase the number of complete initial PMTA bundles, generating costs to firms. In Table 28, we estimate the total costs to firms from PMTA preparation and submission over 20 years. As shown in Table 32, we estimate that the proposed rule would generate $3.27 million in annualized costs to firms at a 3 percent discount rate and $3.52 million in annualized costs to firms at a 7 percent discount rate.

Table 34. Total Cost to Firms from ENDS PMTA Preparation and Submission ($m)

Present Value (3%)	$50.16
Present Value (7%)	$39.85
Annualized Value (3%)	$3.27
Annualized Value (7%)	$3.52

[a] Mean values from simulation.

3. Costs to FDA from PMTA Review

The proposed rule, if finalized, would increase the number of complete initial bundles (see Tables 22 and 23) and reduce the review cost per complete bundle (see Table 29). The net effect would generate costs for FDA to review complete initial bundles. In Table 35, we show the total costs to FDA from PMTA review over 20 years. We estimate that the proposed rule

[26] In our simulation, we assume that the number of affected firms is a uniform random variable between 1,400 and 2,450. We also assume that the percent of firms that are small businesses is a uniform random variable between 83 percent and 85 percent.

would generate $1.03 million in annualized costs at a 3 percent discount rate and $1.10 million in annualized costs at a 7 percent discount rate.

Table 35. Total Cost to FDA from ENDS PMTA Review ($m)

Present Value (3%)	$15.81
Present Value (7%)	$12.45
Annualized Value (3%)	$1.03
Annualized Value (7%)	$1.10

[a] Mean values from simulation.

4. Costs for Originally Regulated Bundles

Because we assume a pre-statutory baseline for originally regulated tobacco products in this analysis, firms seeking marketing orders through the PMTA pathway incur the full costs to prepare PMTA bundles and we incur the full costs to review such PMTA submissions. However, we expect that PMTAs for originally regulated products would be rare. Therefore, we assume that we would receive on average one bundle annually.[27]

Because originally regulated products have been on the market for many years, we expect the burden of preparing and submitting an originally regulated PMTA bundle is lower than that of an ENDS PMTA bundle, which may require new research. Therefore, to estimate the cost of submission and review of originally regulated product bundles, we make the following assumptions.

1) The cost to prepare and submit a bundle falls between the cost to prepare and submit a low complexity[28] e-cigarette bundle (lower bound) and the cost to prepare and submit a low complexity e-liquid bundle (upper bound).
2) Firms only submit original PMTA bundles.
3) The cost to review a bundle equals the cost to review a low complexity bundle.

We request comment on these assumptions, including the assumption that an e-cigarette bundle represents a lower bound on the cost of an originally regulated bundle.

In Table 36, we show our estimate the total cost of premarket review for originally regulated products using the PMTA pathway with a pre-statutory baseline. Based on our assumption that we would receive at most one PMTA bundle per year for an originally regulated product and that the cost to prepare, submit, and review that bundle would fall between the costs for e-cigarette bundles and the costs for e-liquid bundles, we estimate that the mean annualized cost of premarket review for originally regulated bundles would equal $0.27 million at a 3 percent discount rate and at a 7 percent discount rate.

Table 36. Total Cost of Premarket Review for Originally Regulated Products ($m)

[27] In our simulation, we assume that number of PMTA bundles for originally regulated products in a given year is a uniform random variable with a lower bound of 0 and an upper bound of 1.

[28] We estimate the cost to prepare and submit low complexity e-cigarette and e-liquid bundles using data for "low average cost" PMTA bundles from the regulatory impact analysis for the Deeming Rule, adjusted for wages and inflation.

Value	Cost to Prepare and Submit PMTAs[a]	Cost to Review PMTAs[a]	Costs of Deficiency Letters[a]	Total Cost[a]
Present Value (3%)	$2.39	$1.56	$0.21	$4.17
Present Value (7%)	$1.75	$1.13	$0.16	$3.03
Annualized Value (3%)	$0.16	$0.10	$0.01	$0.27
Annualized Value (7%)	$0.15	$0.10	$0.01	$0.27

[a] Mean values from simulation.

5. Costs of Postmarket Reporting

To estimate the cost of postmarket reporting under the proposed rule, we first estimate the number of marketed bundles by year. We assume that firms begin marketing the products in each PMTA bundle as soon as they receive a marketing order, and they continue marketing those products until the end of their profitable life. Given our assumption that firms receive marketing orders for all complete bundles, we estimate the total number of bundles marketed through the PMTA pathway over time as shown in Table 37. These estimates represent the number of bundles with marketing orders through the PMTA pathway on the market in each year.

Table 37. Number Bundles Marketed through the PMTA Pathway over Time

Year[b]	ENDS Bundles[a]	Originally Regulated Bundles[a]
2019	0.00	0.00
2020	0.00	0.25
2021	24.70	0.59
2022	37.10	1.00
2023	51.06	1.50
2024	66.44	2.24
2025	98.47	2.56
2026	70.69	2.80
2027	68.37	2.97
2028	64.42	2.97
2029 and On	51.20	2.97

[a] Mean values from simulation.
[b] Based on our compliance date assumptions as of April 2019.

a. Cost of Periodic Reports

Under the proposed rule, firms would submit periodic reports for products with marketing orders. In general, while we may require in a specific marketing order that a firm make reports more or less frequently, initially we expect to require periodic reports annually. For this analysis, we assume that firms would submit these reports annually, for the complete duration of the product's life. By making this assumption, we likely overestimate the cost of periodic reporting. CTP's Office of Science estimates that it would take firms between 20 and 80

hours[29] to prepare periodic reports for all products in each PMTA bundle. We also estimate that it would take us between 96 and 480 hours to review all periodic reports within a PMTA bundle.[30]

Using the wage for scientific staff, the wage for CTP staff, and the number of marketed bundles from Table 37, we show our estimate of the total cost of periodic reporting to firms and to FDA in Table 38 over 20 years. The mean annualized cost of periodic reporting would equal $1.90 million at a 3 percent discount rate and $1.80 million at a 7 percent discount rate.

Table 38. Total Cost of Periodic Reporting ($m)

Value	Cost to Firms[a]	Cost to FDA[a]	Total Cost[a]
Present Value (3%)	$2.82	$26.35	$29.17
Present Value (7%)	$1.98	$18.47	$20.45
Annualized Value (3%)	$0.18	$1.72	$1.90
Annualized Value (7%)	$0.17	$1.63	$1.80

[a] Mean values from simulation.

b. Cost of Mandatory Adverse Experience Reporting

Under the proposed rule, if finalized, firms would also submit adverse experience reports for tobacco products with marketing orders. Currently firms may voluntarily submit adverse experience reports using FDA Form 3800. The Information Collection Request for this form estimates that mandatory reporting takes 1 hour to complete this form for food products (Ref. 10). Using the composite wage from Table 5 and assuming that it would take 1 hour for tobacco products as well, we estimate that submitting an adverse experience report would cost $72.95. We request comment on this assumption.

We use the number of adverse experience reports submitted to estimate the number of adverse experience reports we would receive for each bundle under the proposed rule, if finalized. In the 23 months from January 2017 to November 2018, we received 86 product problem reports for ENDS and 9 product problem reports for smokeless products[31] (Ref. 11), or 45 annual reports for ENDS (86 product problem reports × 12 months ÷ 23 months) and 5 annual reports for smokeless products (5 product problem reports × 12 months ÷ 23 months). We identified 202 ENDS bundles and 169 smokeless bundles in FDA CTP-licensed Nielsen data (Footnote 18). This suggests that we have received approximately 0.22 product problem reports per ENDS bundle and 0.02 product problem reports per smokeless bundle.

However, voluntary adverse experience databases tend to underreport the total number of adverse experiences. Goldman et al. (1996) found that voluntary drug surveillance systems

[29] In our simulation, we assume that the cost to submit periodic reports is a uniformly distributed random variable with a lower bound of 20 hours and an upper bound of 80 hours.
[30] In our simulation, we assume that the cost to review periodic reports is a uniformly distributed random variable with a lower bound of 96 hours and an upper bound of 480 hours.
[31] Recall from the Benefits section that we use the market for smokeless tobacco products to characterize the market for originally regulated tobacco products that use the PMTA pathway.

underreported adverse events by between 1 percent and 10 percent (Ref. 12)[32]. Therefore, we estimate that, had adverse experience reporting been mandatory, we would have received, on average, an additional 5.43 reports per ENDS bundle and an additional 0.57 reports per smokeless bundle.

Using the estimated number of adverse experience reports, the cost per adverse experience report, and the number of marketed bundles from Table 37, we show our estimate of the total cost of adverse experience reporting in Table 39. We estimate that, over 20 years, the annualized mean cost of adverse experience reporting would equal $21.93 thousand at a 3 percent discount rate and $20.82 thousand at a 7 percent discount rate.

Table 39. Total Cost of Adverse Experience Reporting per Bundle ($ thousands)

Value	ENDS Bundles[a]	Originally Regulated Bundles[a]	Total Cost[a]
Present Value (3%)	$334.47	$1.59	$336.06
Present Value (7%)	$234.89	$1.07	$235.96
Annualized Value (3%)	$21.83	$0.10	$21.93
Annualized Value (7%)	$20.72	$0.09	$20.82

[a] Mean value from simulation.

We do not include the cost to review adverse experience reports in the total cost of adverse experience reporting. We would require periodic reports include summary information on all adverse experiences. Therefore, we assume that the cost to review a periodic report includes the cost to review all adverse experience reports from the year of the report.

6. Costs to Establish Records for SE Exempt and Grandfathered Products

The proposed rule, if finalized, would require that firms maintain records related to SE Exemption Requests and Grandfathered products. We expect that the cost to maintain records would be negligible once firms have established records. For example, we expect the costs of this proposed rule to be negligible for SE Exemption Requests. Firms would have already established the required records when submitting the SE Exemption Request and would only incur small costs to maintain those records. Similarly, we expect the costs of this proposed rule to be negligible for any Grandfathered products that have already submitted Standalone Grandfathered Submissions, because firms would have established the required records when submitting the Standalone Grandfathered Submissions.

The proposed rule would only generate costs to maintain records for any Grandfathered products that firms have not submitted Standalone Grandfathered Submissions. Based on our inspections of manufacturers of finished, originally regulated tobacco products, we estimate that 10 percent of originally regulated products are grandfathered products for which the manufacturer did not submit Standalone Grandfathered Submissions. Given that there are approximately 5,800 originally regulated products listed with FDA, we estimate that firms would establish records for about 580 products under the proposed rule.

[32] In our simulation, we assume that the percent of adverse experience reported voluntary is a uniform random variable with a lower bound of 1 percent and an upper bound of 10 percent.

We estimate that it would take administrative staff approximately 2 hours to collect the required records for a Grandfathered Product without a Standalone Grandfathered Submission. Maintaining records would require minimal effort once identified. Using the wage for administrative staff from Table 5, the total cost to establish records would equal $45,774 (2 hours per product × $39.46 per hour × 580 products). We assume that firms would incur these costs by the effective date of the rule, one year after publication of the final rule. Given this assumption, we show our estimate of the total costs of establishing records over 20 years in Table 40.

We estimate that the annualized cost to establish records for grandfathered products would equal $2.90 thousand at a 3 percent discount rate and $3.77 thousand at a 7 percent discount rate.

Table 40. Cost to Establish Records for Grandfathered Products over 20 Years ($ thousands)[a]

Present Value (3%)	$44.44
Present Value (7%)	$42.78
Annualized Value (3%)	$2.90
Annualized Value (7%)	$3.77

7. Summary of Costs

In Table 41, we estimate the total costs of the proposed rule over 20 years. The total annualized costs would equal $6.76 million at a 3 percent discount rate, with a 90 percent confidence interval ranging from $3.12 million to $11.05 million. The total annualized costs would equal $7.05 million at a 7 percent discount rate, with a 90 percent confidence interval ranging from $3.18 million to $11.65 million.

Table 41. Total Costs of the Proposed Rule over 20 Years ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	$47.79	$103.60	$169.35
Present Value (7%)	$36.09	$79.97	$132.01
Annualized Value (3%)	$3.12	$6.76	$11.05
Annualized Value (7%)	$3.18	$7.05	$11.65

[a] Only mean values sum in simulation results.

G. Distributional Effects

We expect that the proposed rule, if finalized, could generate transfers between tobacco products. In our model, we assume a fixed demand for tobacco products in a given period. Every product on the market captures some share of this demand. To understand the potential transfers from this proposed rule, we consider the transfers created by incomplete, partially complete, and complete bundles under the assumptions in our model.

When a firm submits an incomplete or partially complete bundle, we refuse to accept or refuse to file that bundle. If we refuse to accept or file a bundle the firm submitted during the Deeming compliance period, then we would expect that the firm would remove the products in that bundle from the market. Sales from the products in the bundle transfer to other products

remaining on the market. If we refuse to accept or file a bundle the firm submitted after the end of Deeming compliance period, the products in that bundle would not have already been on the market and no transfer occurs. After a few years, if the firm submits a follow-on bundle and we issue marketing orders for the products in the bundle the firm can introduce or re-introduce (for products marketed before Deeming) the products in the bundle to the market. Sales from other products on the market then transfer to the newly introduced (or reintroduced) products in the bundle.

Based on the assumptions in our analysis, when a firm submits an initial complete bundle, we assume that FDA will issue a marketing order for the products in the bundle. If the firm submitted the bundle during the Deeming compliance period, then we would expect the products in the bundle to stay on the market and no transfer occurs. If the firm submitted the bundle after the Deeming compliance period, then the firm introduces the products in the bundle to the market. Sales from other products on the market transfer to the newly introduced products in the bundle.

Without rulemaking, we expect that most initial bundles submitted by firms would be incomplete or partially complete. With rulemaking, we expect that most initial bundles submitted by firms would be complete. The net transfers from rulemaking would equal the expected increase in profits for submitted bundles as submissions become more complete and products with marketing orders capture more of the tobacco market.

H. International Effects

The requirements of the proposed rule are the same for domestic and foreign firms. We request comment on whether the proposed rule would disproportionately affect foreign PMTA applicants.

I. Alternative Baseline Analysis

In the primary analysis of the proposed rule, we use a pre-statutory baseline for originally regulated products and include the costs of PMTA bundles for originally regulated products. In this uncertainty analysis, we use a post-statutory baseline for originally regulated products. In this baseline, originally regulated products are subject to premarket review through the PMTA pathway.

In Table 42, we estimate the net cost savings of the proposed rule under this alternative baseline. We estimate that annualized net costs savings would equal $5.55 million at a 3 percent discount rate, with a 90 percent confidence interval ranging from $2.60 million to $9.20 million. We estimate that annualized net cost savings would equal $5.65 million at a 7 percent discount rate, with a 90 percent confidence interval ranging from $2.63 million to $9.39 million.

Table 42. Cost Savings of Rulemaking with a Post-Statutory Baseline for Originally Regulated Products ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	$39.91	$85.05	$140.94
Present Value (7%)	$29.79	$64.00	$106.47
Annualized Value (3%)	$2.60	$5.55	$9.20

Annualized Value (7%)	$2.63	$5.65	$9.39

[a] Only mean values sum in simulation results.

In Table 43, we estimate the net costs of the proposed rule under this alternative baseline. We estimate that annualized net costs would equal $6.55 million at a 3 percent discount rate, with a 90 percent confidence interval ranging from $2.86 million to $10.90 million. We estimate that annualized net costs would equal $6.85 million at a 7 percent discount rate, with a 90 percent confidence interval ranging from $2.93 million to $11.51 million.

Table 43. Costs of Rulemaking with a Post-Statutory Baseline for Originally Regulated Products ($m)[a]

Value	5th Percentile	Mean	95th Percentile
Present Value (3%)	$43.84	$100.33	$166.96
Present Value (7%)	$33.25	$77.60	$130.44
Annualized Value (3%)	$2.86	$6.55	$10.90
Annualized Value (7%)	$2.93	$6.85	$11.51

[a] Only mean values sum in simulation results.

J. Analysis of Regulatory Alternatives to the Proposed Rule

As an alternative to this proposed rule, we could publish the format and content requirements for PMTAs without including requirements for postmarket reporting, including periodic reporting and mandatory adverse experience reporting. Based on our assumption that bundles are profitable for between 5 and 20 years, we estimate that the annualized total costs of postmarket reporting are $1.93 million at a 3 percent discount rate and $1.82 million at a 7 percent discount rate. If firms market bundles with marketing orders through the PMTA pathway for longer than 20 years, then these costs would be higher. Eliminating the requirement for postmarket reporting would reduce the net costs of the proposed rule.

Although we lack information to quantify the benefits of postmarket reporting, we expect that periodic reports and mandatory adverse experience reports would provide us with important information about unexpected adverse health outcomes from marketed tobacco products. Thus, removing postmarket reporting requirements would eliminate any potential public health benefits of postmarket reporting which could outweigh the potential cost-savings of this alternative.

III. Initial Small Entity Analysis

The Regulatory Flexibility Act requires Agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. The Small Business Administration (SBA) considers tobacco manufacturing entities with less than 1,500 employees as small. Data from 2012 from the US Census Bureau[33] shows that SBA would consider 96 percent of tobacco manufacturers as small entities. Data from 2018 from Dun and Bradstreet

[33] From the 2012 Statistics of U.S. Businesses for NAICS Code 3122, available at https://www.census.gov/data/datasets/2012/econ/susb/2012-susb.html

matched to TRLM data suggests that SBA would consider 84 percent of tobacco manufacturers as small entities.

Table 44. Percent of Firms and Average Annual Revenues per Firm by Employment Size based on Census Data

Employment Size	Percent of Firms	Average Annual Revenues per Firm (millions of 2017$)
0 to 19 Employees	51%	$4.37
20 to 99 Employees	29%	$26.24
100 to 499 Employees	10%	$183.90
500 to 999 Employees	3%	Unavailable
1,000 to 1,499 Employees	3%	$825.43
All Small	96%	$56.69

This rulemaking would primarily impact those firms that remain on the market following the Deeming compliance period. The Deeming Rule will cause many existing firms to exit the market. Given our assumptions about the Deeming compliance period, we expect the Deeming Rule would also create significant market consolidation for deemed tobacco products by 2020. Some small manufacturers may exit the market or merge with other manufacturers to afford the compliance costs associated with the Deeming Rule. Other small manufacturers may expand production and increase their market share as their competition exits the market.

We assume that all small tobacco manufacturers would incur average one-time costs to read and understand the rule of $1,620 with annualized costs of $106 at 3 percent discount rate and $143 at a 7 percent discount rate. We base these estimates on an assumption that two lawyers would read and understand the rule at all small manufacturers. However, we expect that most vape stores and specialty tobacco product manufacturers would learn about the rule from industry associations, rather than paying a lawyer to read the rule. Therefore, we likely overestimate the cost to read and understand the rule for many small tobacco manufacturers.

Some small manufacturers of grandfathered products without Standalone Grandfathered Determinations would incur average one-time costs to establish records of $78 per product. We do not know how many grandfathered products without Standalone Grandfathered Determinations each small entity manufactures. However, if we assume that such small manufacturers would each establish records for 10 products on average, then the total one-time costs per small entity to establish records would equal $789, with annualized costs of $50 at a 3 percent discount rate and $65 at a 7 percent discount rate.

Manufacturers that submit ENDS PMTA bundles would benefit from the proposed rule, if finalized. Submitted bundles would receive marketing orders through the PMTA pathway earlier with rulemaking than without rulemaking, increasing lifetime profits for the ENDS products included in the submitted bundles. In Table 45, we present the distribution of the net gains from rulemaking per submitted ENDS bundle. The net impact of the rule per bundle for all submitted ENDS bundles is positive.

Table 45. Percent of Submitted ENDS Bundles with Net Gains over Product Life, by Magnitude of Net Gains

Net Gains per Bundle	E-Liquids	E-Cigarettes
Less than $1m	41%	45%
Between $1m and $10m	30%	37%
Between $10m and $50m	21%	13%
Greater than $50m	9%	5%
Total	100%	100%

Manufacturers of originally regulated bundles would incur costs to prepare and submit PMTAs and the costs of postmarket reporting. The total annualized cost of submitting an originally regulated bundle would equal $23 thousand per bundle at a 3 percent discount rate and $30 thousand at a 7 percent discount rate. Such manufacturers of would also incur profit losses from getting on the market later with rulemaking than without rulemaking, though we cannot estimate these losses. For the smallest entities, these costs represent at least 0.5 percent of annual revenue at a 3 percent discount rate ($0.02 million in annualized costs ÷ $4.37 million in annual revenue) and at least 0.7 percent of annual revenue at a 7 percent discount rate ($0.03 million in annualized costs ÷ $4.37 million in annual revenue. However, such submissions would be rare. We estimate that we would receive, on average, 1 bundle every 2 years, impacting at most 10 small entities over 20 years. Furthermore, firms would only submit originally regulated bundles if the expected lifetime profits from submission were greater than the expected lifetime cost of submission. Therefore, while this cost may be significant for some small entities, we do not anticipate that it would affect a substantial number of small entities.

To summarize, most small entities would either benefit from the proposed rule or would incur small annualized costs of approximately $200. A few small entities may incur significant costs to submit PMTA bundles for originally regulated tobacco products, but these submissions would be rare and would affect very few small entities. For these reasons, we estimate that the rule would not have a significant economic impact on small entities. Thus, we proposed to certify that the proposed rule would not have a significant economic impact on a substantial number of small entities.

IV. References

1. **U.S. Food and Drug Administration**, 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 81 FR 28973. 2016. Available from: https://www.gpo.gov/fdsys/pkg/FR-2016-05-10/pdf/2016-10685.pdf.
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3. **U.S. Food and Drug Administration**, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry. 2019. Available from: https://www.fda.gov/media/127853/download.
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V. Technical Appendix

A. Defining a PMTA Bundle

We define a PMTA bundle using Nielsen RMS data from January 2018 to August 2018 from the xAOC and Convenience channels, where xAOC stands for "expanded all outlets combined" (see Footnote 18). This data includes product characteristics and weekly sales at the UPC-level in a national sample of retail establishments that includes:

- Food, drug, dollar, and club stores;
- Mass merchandisers;
- Military commissaries; and,
- Convenience stores.

By using Nielsen RMS data to estimate the number of bundles that would submit PMTAs, we inherently assume that firms would not submit bundles for any tobacco products that do not appear in Nielsen data. Moreover, we expect that only the ENDS products with the highest market share in the ENDS market would be sold in the retail establishments included in Nielsen. Firms manufacturing these products are more likely to have the resources necessary to prepare and submit a PMTA bundle.

We restrict our sample to electronic vapor products (the Nielsen product category). We then classify each UPC in this category of products as an "e-cigarette" or an "e-liquid" based on the product type listed in Nielsen RMS data. Specifically, we define "e-cigarette" to include disposable electronic cigarettes, cigars, hookahs, and pipes, as well as electronic cigarette batteries and kits. "E-liquids" include liquid refills for electronic cigarettes and non-liquid refills (typically cartridges containing e-liquids) for electronic cigarettes. Then, we define a bundle in our data as a unique combination of three variables:

- Major brand, which is the major brand name listed on a product's label;
- Brand extension, which we find often identifies a specific model of a product marketed by the major brand; and.
- Product type (i.e., e-cigarette vs. e-liquid).

By using this definition of a bundle, we will underestimate the number of bundles currently on the market to the extent that the brand extension does not capture different models marketed by a brand. We will overestimate the number of bundles currently on the market if different brand extensions under the same brand or different brands with the same manufacturer represent products that may be submitted in a single bundle.

B. Estimating Annual Bundle Profits

To estimate annual bundle profits, we first aggregate the weekly sales data for each UPC in Nielsen RMS data to the bundle level. Next, we adjust the annual sales estimates upwards to account for sales in non-Nielsen channels. Euromonitor's 2018 report on Tobacco in the U.S. includes national-level estimates of sales in the ENDS market through all channels. By comparing the total sales in Nielsen and the total sales in Euromonitor for ENDS products, we estimate that Nielsen captures approximately 58 percent of the total sales in the ENDS market.

We therefore assume that the national sales of each bundle in our Nielsen sample are double the sales reporting in the Nielsen data.

Many potential PMTA bundles are likely marketed exclusively in non-Nielsen channels, like vape shops. By assuming that bundles in Nielsen RMS data capture the remaining 42 percent of sales in the ENDS market, including sales to bundles marketed exclusively through non-Nielsen channel, we likely overestimate the 2018 sales of each bundle in our sample. However, we assume that only firms with bundles in the Nielsen data can afford to submit PMTAs and would likely capture the market share from other bundles from firms unable to submit PMTAs.

Finally, we convert sales for each bundle into profits. A report on e-cigarettes in the EU[34] estimates that profits for e-cigarettes are approximately 40 percent of sales. An article about JUUL,[35] the leader in the ENDS market, estimates that JUUL profits are approximately 70 percent of sales. To capture this uncertainty, we assume that the profit margin for ENDS products is a uniform random variable m with a lower bound of 40 percent and an upper bound of 70 percent. Then, the profits for each individual bundle is the national-level sales times the random profit margin.

To summarize, the profits π_j of an individual bundle j can be expressed as:

$$\pi_j = 2 \cdot m \cdot \frac{52}{32} \cdot \sum_{t=1}^{32} \sum_{i=1}^{N_j} s_{ijt}$$

Where s_{ijt} is the Nielsen sales of UPC i in bundle j at week t and N_j is the total number of UPCs in bundle j.

We use the same method to estimate the total profits from flavored ENDS in a bundle. If f_{ij} equals 1 for UPC i in bundle j is a flavored ENDS, as defined in section II of this document, and 0 otherwise, then the total profits from flavored ENDS π_j^F in a bundle j is given by:

$$\pi_j^F = 2 \cdot m \cdot \frac{52}{32} \cdot \sum_{t=1}^{32} \sum_{i=1}^{N_j} s_{ijt} \cdot f_{ij}$$

C. Estimating Expected Net Present Value Profits from Submission with and without Rulemaking

Firms decide whether to submit a PMTA bundle by comparing the expected net present value of the benefits of submitting that bundle (i.e., lifetime profits) to the expected net present value of the costs of submitting that bundle. First, we calculate the expected net present value of profits for each bundle with and without rulemaking.

[34] https://www.retaildata.co.uk/news-updates/e-cigarettes-high-margins-high-potential/
[35] https://www.axios.com/numbers-juul-investor-appeal-vaping-22c0a2f9-beb1-4a48-acee-5da64e3e2f82.html

We use discount rates of 3 percent and 7 percent to represent the social discount rate (following OMB Circular A-4 guidelines). However, firms in the tobacco industry likely make investment decisions based on the cost of capital. Damodoran (2019)[36] estimates that the cost of capital in the tobacco industry in the U.S. is 8.97 percent, while estimates of the cost of capital for individual tobacco companies range from 7 percent to 11 percent.[37] We assume that the cost of capital is a random variable following a triangle distribution with a lower bound of 7 percent, a mean of 8.97 percent, and an upper bound of 11 percent. We then use this simulated cost of capital to approximate the discount rate used by firms when deciding whether to submit a PMTA bundle.

In our analysis, we assume that the average life of a tobacco product with a marketing order is a uniform random integer between 5 and 20 years, and that all products within a bundle would have the same product life. Under the Tobacco Control Act, modifications to tobacco products represent new tobacco products, and new tobacco products must follow the PMTA, SE, or SE Exemption pathways to obtain marketing authorization.

The present value profits of a bundle over its life depend on the completeness of the bundle upon initial submission. In our model, complete bundles receive marketing orders in the same year that firms submit them, while partially complete and incomplete bundles only receive marketing orders after submitting follow-on bundles. We illustrate the flow of profits over time in Appendix Table 1 for the random draw where bundle life is the lower bound, 5 years, and the time to follow-on submission is 2 years. Bundles that are complete at initial submission begin earning profits in the year of initial submission (year 0), while bundles that are partially complete or incomplete begin earning profits 2 full years after initial review (year 3).[38]

Appendix Table 1. Years of Profit for Bundles by Completeness

Time	Complete	Partially Complete or Incomplete
0 (Initial Submission)	1	0
1	1	0
2	1	0
3	1	1
4	1	1
5	0	1
6	0	1
7	0	1

We discount the total profit over the life of the bundle to the time that the firm submits the PMTA bundle. In the scenario presented in Appendix Table 1, complete bundles earn 4.24 years of discounted profits over their life, while partially complete or incomplete bundles earn 3.28 years of discounted profits.

[36] http://people.stern.nyu.edu/adamodar/New_Home_Page/datafile/wacc.htm
[37] https://finbox.com/PM/explorer/wacc, accessed June 27, 2019.
[38] As illustrated in Appendix Table 1, we conduct our analysis in increments of full calendar years. We assume that if a bundle earns any profits in a year, then it earns a full year of profits. We use this approach to simplify the analysis.

We assume that total profits and flavored profits are constant over time for each bundle. In making this assumption, we do not account for future trends in the ENDS market. Moreover, given the pending changes to the regulatory landscape for ENDS, we cannot predict how sales of individual bundles will change in the future. Given this assumption, the total profits over a bundle's life, denoted by $\Pi_j(x)$, for a given level of completeness at initial submission x are given by:

$$\Pi_j(x) = \pi_j \cdot \sum_{t=0}^{\infty} \frac{I(x,t)}{(1+\delta)^t}$$

Where δ is the firm's discount rate and the function $I(x,t)$ equals 1 if a bundle of completeness x earns profits t years after initial submission and 0 otherwise.

Finally, knowingly submitting a partially complete or incomplete bundle is not profit maximizing behavior in our model for most firms. Thus, we assume that the completeness of a PMTA bundle is unknown to the firm. This assumption is consistent with our experience with potential PMTA applicants to date, who frequently request more guidance on the format and content requirements for PMTAs. In addition, the net profits that a firm can earn for an initially complete bundle are, in general, higher than the net profits that a firm can earn for an initially partially complete or incomplete bundle.

In our primary analysis, we describe the completeness probability distributions with and without rulemaking. Suppose that p_0, p_1, and p_2 be the probability that a bundle is complete, partially complete, and incomplete at the time of initial submission, and let x_0, x_1, and x_2 indicates that a bundle is complete, partially complete, and incomplete. Then the total expected profits from submission $E[\Pi_j]$ of a PMTA bundle j are given by:

$$E[\Pi_j] = p_0 \cdot \Pi_j(x_0) + p_1 \cdot \Pi_j(x_1) + p_2 \cdot \Pi_j(x_2)$$

Note that the probabilities p_0, p_1, and p_2 would change because of this rulemaking. Since we predict that the probability p_0 would be higher with rulemaking than in the baseline, the expected profits from submission would be higher with rulemaking than in the baseline.

D. Estimating Expected Net Present Value Costs from Submission with and without Rulemaking

In Appendix Table 2, we describe the types of costs that a firm would incur if they submitted a PMTA both with and without rulemaking. When deciding whether to submit a PMTA bundle, the firm compares expected profits to the total costs of submitting a bundle, from the time of initial submission to the end of the bundle's life. In this section, we discuss how we estimate the expected net present value of submission.

Appendix Table 2. Types of Incremental Costs of Submitting a PMTA

Type of Cost	Incurred in the Baseline	Incurred with Rulemaking
Cost of PMTA Preparation and Submission	Yes	Yes
Cost of Periodic Reporting	No	Yes
Cost of Adverse Experience Reporting	No	Yes

The timing of costs depends on the completeness of a bundle *at the time of initial submission*. In Appendix Table 3, we illustrate the timing of submission costs by bundle completeness at the time of initial submission, using the same example used in Appendix Table 1. Note that, for simplicity, we assume firms make this decision at the time of initial submission.

For a bundle that is complete at the time of initial submission, we assume that the firm receives a marketing order at the time of initial submission. Then, the firm incurs the cost of the initial submission and postmarket reporting costs in the year of submission, then incurs the costs of postmarket reporting for the remainder of the bundle's profitable life. For a bundle that is partially complete or incomplete at the time of initial submission, the firm incurs only the cost of the initial submission at the time of initial submission. The firm incurs the cost of follow-on submission and postmarket reporting at the time of follow-on submission, then incurs the cost of postmarket reporting for the remainder of the bundle's profitable life.

Appendix Table 3. Timing of Costs by Bundle Completeness

Time	Complete Initial Submission	Partially Complete or Incomplete Initial Submission
0 (Initial Submission)	Initial Submission Postmarket Reporting[a]	Initial Submission
1	Postmarket Reporting[a]	None
2	Postmarket Reporting[a]	None
3	Postmarket Reporting[a]	Follow-On Submission Postmarket Reporting[z]
4	Postmarket Reporting[z]	Postmarket Reporting[z]
5	None	Postmarket Reporting[z]
6	None	Postmarket Reporting[z]
7	None	Postmarket Reporting[z]

[a] Incurred with rulemaking only.

We discount these costs, described in detail in the primary analysis, back to the time of the initial submission for each level of bundle completeness. Let $C_j(x)$ be the net present value of submitting a bundle j, relative to the time of initial submission, for a given level of

completeness x. Using the definitions of p_0, p_1, and p_2 and the definitions of x_0, x_1, and x_2 from section C, then the expected cost of submitting a PMTA bundle $E[C_j]$ is given by:

$$E[C_j] = p_0 C_j(x_0) + p_1 C_j(x_1) + p_2 C_j(x_2)$$

Both the cost function $C_j(x)$ and the probability of each level of completeness would change because of this rulemaking. Due to the time value of money, the cost to submit an initially complete bundle exceeds the cost to submit an initially incomplete or partially complete bundle. If, as we assume in our analysis, the probability p_0 would increase because of this rulemaking, then the expected cost of submitting a bundle would increase, all else equal. Postmarket reporting requirements with this rulemaking would also increase the expected cost of submitting a bundle.

E. Firm Decisions During the Deeming Compliance Period

In our model, we assume an effective date of 2020 for the final rule and that firms would initially comply with the Deeming rule by submitting bundles by the end of 2020. The firm would decide whether to submit a PMTA bundle or discontinue marketing the bundle of products.

If the firm submits a PMTA bundle, its net profits for the bundle would equal $E[\Pi_j] - E[C_j]$. If the firm does not submit a PMTA bundle, its net profits for the bundle would equal 0. Therefore, the firm will submit a PMTA bundle if $E[\Pi_j] - E[C_j] > 0$.

For e-cigarettes, our model will overestimate the number of bundles submitted during the deeming compliance period because we expect that some of these bundles are eligible to receive marketing authorization through the SE pathway. We cannot predict which bundles will use the PMTA pathway and which bundles will use the SE pathway. However, we expect that 78 percent of e-cigarettes will use the PMTA pathway.[39] We adjust the total number of e-cigarette bundles downward to account for use of the SE pathway.

In our primary analysis, we report the mean number of bundles we expect firms to submit with and without regulatory action. We note the following observations about the number of bundles and the sensitivity of our estimates to our assumptions:

- We find that it is never optimal for a firm to submit a bundle before the deeming compliance date, because firms can continue to earn profits without submitting a bundle.
- We estimate that while the number of bundles submitted during the deeming compliance period increases as the length of product life increases, our estimates are relatively insensitive to the length of the product life.

[39] Based on the final regulatory impact analysis for the Deeming Final Rule, available at https://www.fda.gov/about-fda/economic-impact-analyses-fda-regulations/summary-deeming-tobacco-products-be-subject-food-drug-and-cosmetic-act-amended-family-smoking.

- We estimate that while the number of bundles submitted during the deeming compliance period increases as the average profit margin increases, our estimates are relatively insensitive to the profit margin.

1. Treatment of Market Consolidation from Deeming

The final regulatory impact analysis for the Deeming Rule predicts a significant amount of market consolidation in response to that rule's implementation. Our analysis accounts for three types of market consolidation in response to the Deeming Rule. These assumptions parallel the assumption in the regulatory impact analysis for the Deeming rule that the rule would cause vape shops to cease manufacturing activities.

First, we assume that firms do not submit bundles for any products that are not marketed through Nielsen channels and that bundles in Nielsen capture the 42 percent of sales in the ENDS market not included in Nielsen data.

Second, we use a relatively broad data definition of a "bundle" of products, ignoring some differentiating product characteristics that may denote unique bundles, and assume that firms make submission decisions based on profits of that bundle. If a Nielsen-identified brand extension covers multiple potential PMTA bundles of the same product type, then our definition of a bundle implicitly assumes that firms would only submit one PMTA bundles.

Third, we explicitly model the decision of firms to submit PMTA bundles. In our analysis, firms only submit bundles with expected profits from submission that are greater than the expected costs of submission. Under this assumption, firms would remove from the market any bundles with low expected profits.

Our model assumes static demand for tobacco and nicotine products and does not account for expected gains in profits to submitted bundles from Nielsen covered retail channels as firms remove other bundles *in Nielsen* covered retail channels from the market. Estimating the equilibrium number of submitted bundles when firms consider this form of market consolidation is a complicated modelling exercise beyond the scope of this analysis. If large gains in profits exist, then our analysis underestimates the number of bundles submitted during the Deeming compliance period.

F. Number of Bundles After the Deeming Compliance Period

To estimate the number of bundles submitted annually after the deeming compliance period, we use information from the final regulatory impact analysis for the Deeming Rule. In Appendix Table 4, we summarize the information from that analysis used to estimate the annual number of bundles submitted after the deeming compliance period.

Appendix Table 4. Information from the Deeming Rule Final Regulatory Impact Analysis used to Estimate the Annual Number of Bundles After the Deeming Compliance Period

	Low Estimate	Primary Estimate	High Estimate
E-Liquid Products Seeking Marketing Authorization	56	127	225
E-Cigarette Products Seeking Marketing Authorization	17	28	42

% of E-Liquid Products using the PMTA Pathway		40%	
% of E-Cigarette Products using the PMTA Pathway		35%	
Average Products per E-Liquid Bundle		8.7	
Average Products per E-Cigarette Bundle		4.2	

We assume that the number of e-liquid products initially seeking marketing authorization in a given year t after the deeming compliance period, P_t^E, follows a triangle distribution with a lower bound of 56, a mean of 127, and an upper bound of 225. Of these products, approximately 40 percent would seek marketing authorization through the PMTA pathway, while the remaining would utilize other pathways. Based on estimates from Nielsen RMS data (see Footnote 18), we assume that firms would submit bundles through the PMTA pathway with approximately 8.7 products in each bundle. Then, the annual number of e-liquid bundles submitted after the deeming compliance period, E_t', is given by:

$$E_t' = P_t^E \cdot \frac{0.40}{8.7}$$

We may overestimate the number of e-liquid bundles submitted after the Deeming compliance period to the extent that e-liquid bundles could include more products per bundle on average. Similarly, based on Appendix Table 4, the annual number of e-cigarette bundles submitted after the deeming compliance period, D_t', is given by:

$$D_t' = P_t^D \cdot \frac{0.35}{4.2}$$

where P_t^D equals the number of e-cigarette products seeking marketing authorization in a given year t after the deeming compliance period. By drawing P_t^E and P_t^D separately for each year, we assume that the number of products seeking marketing authorization in a given year t is independent of the number of products seeking marketing authorization in all other years.

The estimates from the Deeming Rule final regulatory impact analysis do not account for completeness of PMTAs and instead assumed that all PMTAs would be complete upon initial submission. Because we expect that the proposed rule, if finalized, would improve the completeness of PMTA bundles and, consequently, provide greater incentives for firms to submit PMTA bundles, we assume that E_t' and D_t' represent the number of submitted bundles *with rulemaking.*

To estimate the baseline number of submitted bundles, we adjust E_t and D_t, based on the total number of bundles submitted during the Deeming compliance period. To illustrate, let E_{DCP} be the total number of bundles submitted during the deeming compliance period in the baseline and let E_{DCP}' be the total number of bundles submitted during the deeming compliance period with rulemaking. Then, we assume that the *baseline* number of bundles submitted in year t after the deeming compliance period, E_t, would equal:

$$E_t = E'_t \cdot \frac{E_{DCP}}{E'_{DCP}}$$

Therefore, if rulemaking would not impact the total number of submissions during the deeming compliance period, then $E_t = E'_t$. If rulemaking would increase the total number of submissions during the deeming compliance period, then $E_t < E'_t$. If rulemaking would decrease the total number of submissions during the deeming compliance period, then $E_t > E'_t$.

Similarly, for e-cigarettes, the baseline number of bundles submitted in year t after the deeming compliance period, represented by D_t, would equal:

$$D_t = D'_t \cdot \frac{D_{DCP}}{D'_{DCP}}$$

Where D_{DCP} is the total number of e-cigarette bundles submitted during the Deeming compliance period in the baseline and D'_{DCP} is the number of e-cigarette bundles submitted during the Deeming compliance period with rulemaking.