PREMARKET TOBACCO PRODUCT APPLICATION (PMTA) REVIEW PATHWAY

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AGENDA

- Introduction to Marketing Pathways for New Tobacco Products
- PMTA Statutory Requirements
- Review Process
  - Presubmission meeting
  - Acceptance
  - Filing
  - Review and Action
  - Postmarket Reporting
- Metrics
- Key Features
- Helpful Resources

INTRODUCTION TO MARKETING PATHWAYS FOR NEW TOBACCO PRODUCTS

MARKETING PATHWAYS FOR NEW TOBACCO PRODUCTS

- There are three pathways available to bring a new tobacco product to market in the United States:
  - Premarket Tobacco Product Applications (PMTAs)
  - Substantial Equivalence (SE) Reports
  - Requests for Exemption from Substantial Equivalence (EX REQs)

- The final **deeming rule** extended FDA's tobacco product authorities to all products, other than accessories of deemed tobacco products, that meet the statutory definition of "tobacco product" in section 201(rr) of the FD&C Act (21 U.S.C. 321(rr))

STATUTORY REQUIREMENTS, SECTION 910

STATUTORY REQUIREMENTS

- Under section 910(a)(2) of the Federal Food, Drug, and Cosmetic Act, an order is required for a new tobacco product to be introduced and legally marketed in the United States

- PMTA may be the primary pathway to market a new tobacco product

- At this time, FDA intends to limit enforcement of the requirements of section 910 to finished tobacco products, including components and parts of deemed products sold or distributed separately for consumer use. FDA does not, at this time, intend to enforce these requirements for components and parts of deemed products that are sold or distributed solely for further manufacturing into finished tobacco products, and not sold separately to the consumer

STATUTORY REQUIREMENTS

- The standard required to be met for a PMTA is if marketing of the product is "appropriate for the protection of public health," section 910(c)(4)
  - Considers risks and benefits to the population as a whole:
    - Impact on cessation
    - Impact on initiation
- The product must conform to requirements of section 906(e) (manufacturing practices) which apply (if any)
- The proposed labeling must not be false or misleading
- The product must conform to product standards under section 907 which apply (if any), or must contain an adequate justification for such deviations

PMTA REVIEW PROCESS

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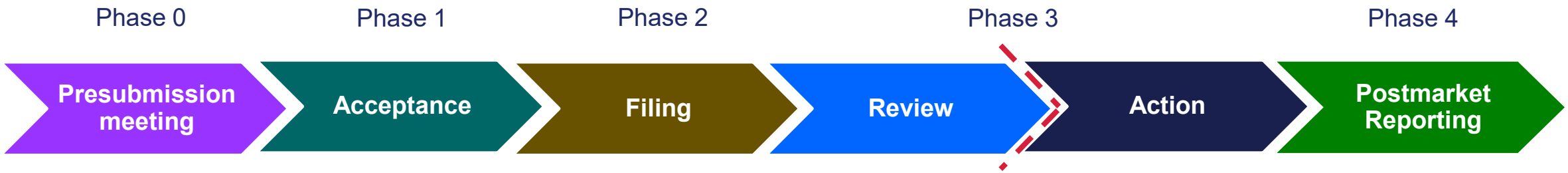


PRESUBMISSION MEETING (PHASE 0)

- Presubmission Meeting
  - Forum to discuss and receive feedback prior to submitting your application
  - Most useful to be held well in advance of the planned pre-market submission
  - May result in a more complete application

See: Meetings with Industry and Investigators on the Research and Development of Tobacco Products (Revised*) (Revised July 2016): Guidance for Industry and Investigators

Presubmission meeting

ACCEPTANCE (PHASE 1)

- Ensure the product falls under CTP jurisdiction
- Confirm the regulatory requirements of an application are included in the submission

See: Final Rule - Refuse To Accept Procedures for Premarket Tobacco Product Submissions

Acceptance

ACCEPTANCE CRITERIA FOR ALL MARKETING PATHWAYS

- In accordance with 21 CFR, 1105.10, FDA will refuse to accept an application for review (PMTA, MRTPA, SE, or EX), if any of the following apply:

1) The submission does not pertain to a tobacco product	6) The submission is from a foreign applicant and does not identify an authorized U.S. agent
2) The submission is not in English or does not contain complete English translations	7) The submission does not contain required FDA forms
3) If submitted electronically, the submission is in a format FDA cannot process, read, review, and archive	8) The type of submission is not identified
4) The submission does not contain contact information, including applicant's name and address	9) The submission does not contain a signature of a responsible official authorized to represent an applicant
5) The submission does not contain product identifying information	10) For all submission types (excluding abbreviated reports), the submission does not include a valid claim of categorical exclusion or an environmental assessment

Acceptance

PRODUCT IDENTIFICATION

- In accordance with (21 CFR § 1105.10(a)(7)), FDA will refuse to accept an application for review if full identification **of the new tobacco product** is not provided; this includes the following criteria:
  - Name of the manufacturer of the new product
  - Product Name
  - Product Category
  - Product Sub-Category
  - Package Type
  - Package Quantity
  - Characterizing Flavor

- If the product does not have a listed product property (e.g., characterizing flavor for a battery), state "none" for that property

Acceptance

PRODUCT IDENTIFICATION

- This table provides an example of full ID for a closed e-liquid, in addition to the name of the manufacturer of the new tobacco product

New Tobacco Product	
Product Name	Product A
Product Category	ENDS (Electronic Nicotine Delivery System)
Product Sub-Category	Closed e-liquid
Package Type	Box
Package Quantity	1 cartridge
Characterizing Flavor	Tobacco
E-liquid Volume	1.0 mL
Nicotine Concentration	5 mg/mL
PG/VG ratio	50/50
Additional Properties	

Acceptance

PRODUCT IDENTIFICATION

New Tobacco Product	
Product Name	Product B
Product Category	ENDS (Electronic Nicotine Delivery System)
Product Sub-Category	Open e-cigarette
Package Type	Box
Package Quantity	1 e-cigarette
Characterizing Flavor	None
Length	75 mm
Diameter	10 mm
E-Liquid Volume	2 mL
Wattage	200 W
Battery Capacity	500 milliampere hours (mAh)
Additional Properties	

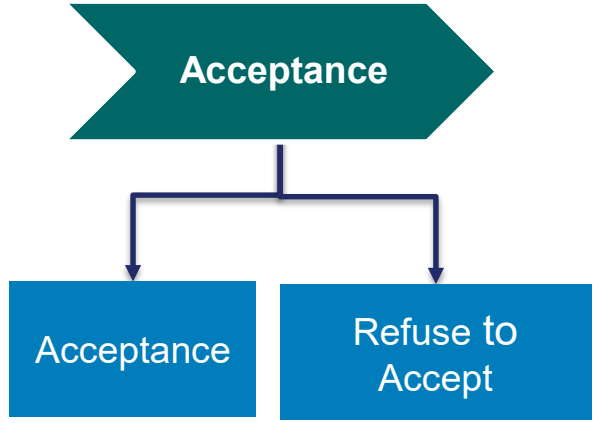
Acceptance

ACCEPTANCE (PHASE 1)

- Expected outcome:
  - Acceptance

    or
  - Refuse to Accept

- If the application is accepted, it moves to the Filing phase



FILING (PHASE 2)

1. Full reports of all information, published or known to, or which should reasonably be known to, the applicant, concerning investigations which have been made to show the health risks of such tobacco product and whether such tobacco product presents less risk than other tobacco products

2. A full statement of the components, ingredients, additives, and properties, and of the principle or principles of operation, of such tobacco product

3. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such tobacco product

Filing

FILING (PHASE 2) (continued)

4. An identifying reference to any tobacco product standard under section 907 which would be applicable to any aspect of such tobacco product, and either adequate information to show that such aspect of such tobacco product fully meets such tobacco product standard or adequate information to justify any deviation from such standard

5. Such samples of such tobacco product and of components thereof as the Secretary may reasonably require

6. Specimens of the labeling proposed to be used for such tobacco product

7. Such other information relevant to the subject matter of the application as the Secretary may require

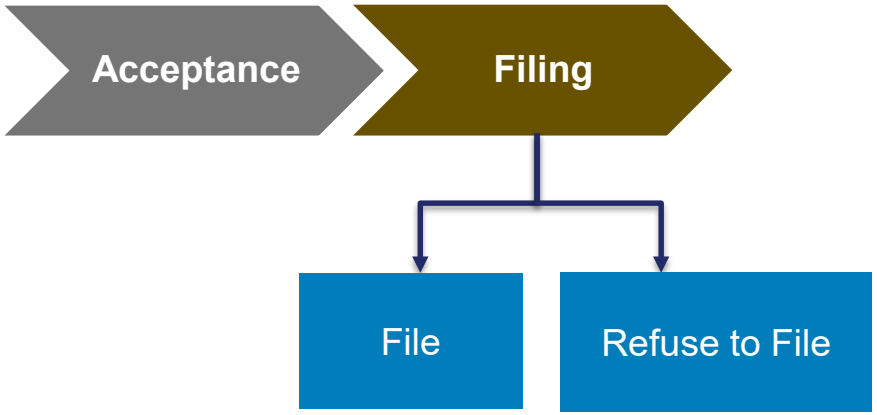
Filing

FILING (PHASE 2) (continued)

- Expected outcome:
  - Filing

    or
  - Refuse to File

- If the application is filed, it moves to the Substantive Review phase



SUBSTANTIVE REVIEW (PHASE 3)

- Multi-disciplinary approach to determine if marketing the new product is appropriate for the protection of public health and can receive an order for the introduction or delivery for introduction into interstate commerce

- Conduct inspections, as appropriate
  - Clinical/Nonclinical
  - Manufacturing

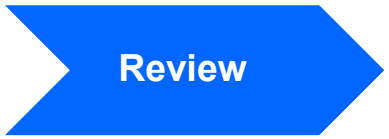
- Test samples, as appropriate

- Determine whether application should go to the Tobacco Products Scientific Advisory Committee (TPSAC)

Review

DEFICIENCIES AND AMENDMENTS (PHASE 3)

- If FDA has questions or identifies additional information needed to render a decision, FDA may choose to issue a Deficiency Letter. The applicant can submit an amendment in response to the Deficiency Letter
- If the applicant submits a **major amendment** to their application, either at FDA's request or on its own initiative, a **new 180 day review period** would begin on the date which FDA receives the major amendment
  - FDA considers major amendments to be those that will require substantial review time. Examples of major amendments include: new data from a previously unreported study, detailed new analyses of previously submitted data, or required necessary information that was previously omitted
- FDA is *not* obligated to review unsolicited amendments



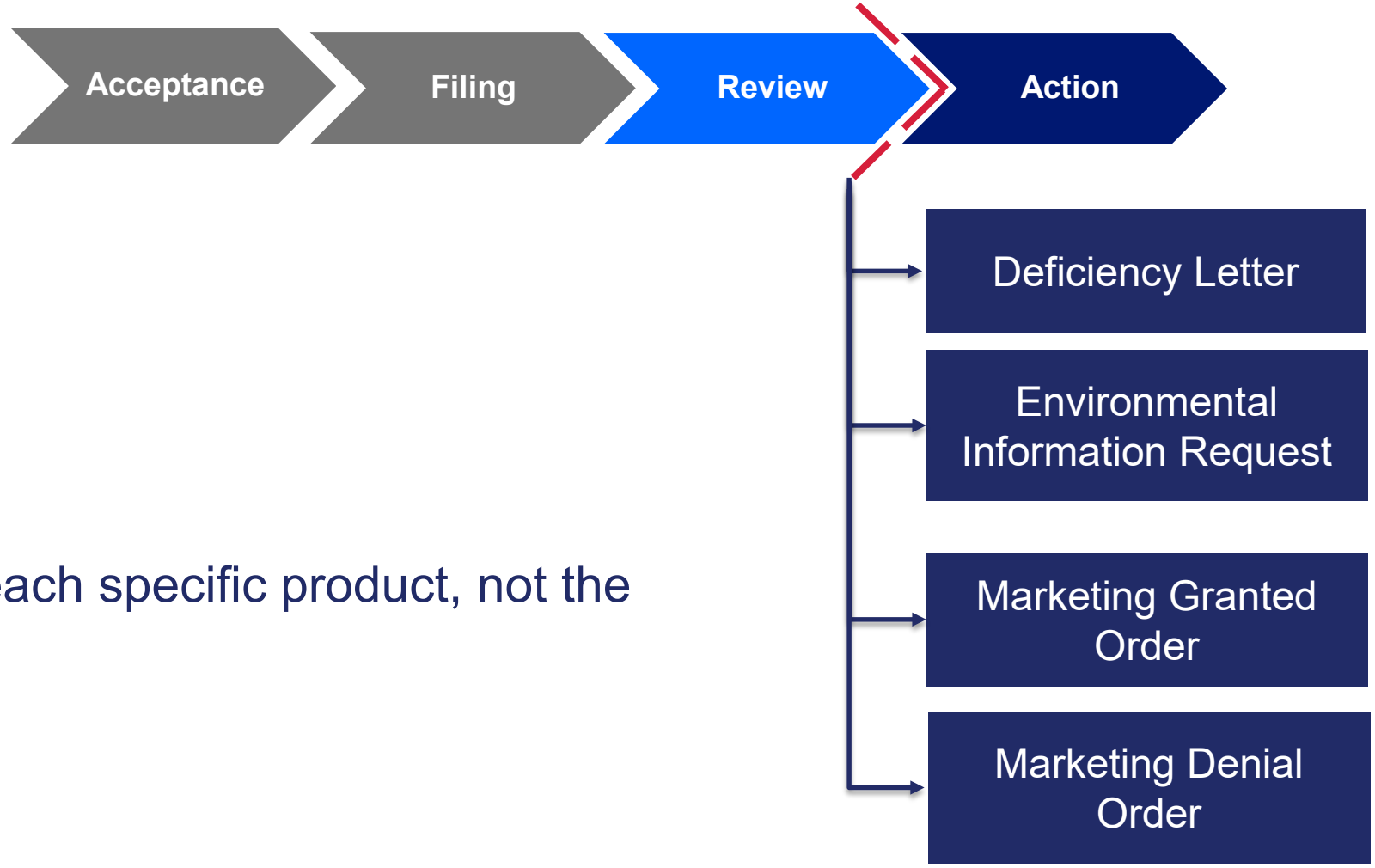
ACTION (PHASE 3)

- **Action result**

  - Marketing Granted Order

    or

  - Marketing Denial Order



- A decision will be made on each specific product, not the submission

POSTMARKET REPORTING (PHASE 4)

- Postmarket reporting, if appropriate, will be included in the Marketing Granted Order letter
  - An order authorizing marketing under section 910(c)(1)(A)(i) of the FD&C Act may require that the sale and distribution of the tobacco product be restricted
  - FDA may require that you establish and maintain certain records and make certain reports available to FDA
  - Postmarket reports will vary based on submission and may include:
    - Serious or Unexpected Adverse Experience Reporting
    - Manufacturing Deviations
    - Annual Reporting

METRICS, KEY FEATURES, AND RESOURCES

WITHDRAWAL OF AN APPLICATION

- Applicants may withdraw an application at any time prior to an action by CTP
  - If a withdrawal is requested, CTP issues a letter acknowledging the withdrawal request
  - A withdrawal is an action that closes the application

PMTA APPLICATIONS BY PRODUCT CATEGORY: STATUTORILY REGULATED PRODUCTS

	Received FY 19	Open FY 19	Closed* FY 19				
			Marketing Granted	Marketing Denial	RTF	RTA	Withdrawn
Cigarettes	4	2	0	0	2	0	0
Roll Your Own	0	0	0	0	0	0	0
Smokeless	0	0	0	0	0	0	0
Total	4	2	2				

* Closed means CTP has taken an action on an application. Closed includes refuse-to-accept, refuse-to-file, withdrawn, closure due to administrative issues, environmental information request letter, predicate advice letter, removed from review, or issuance of order letter as applicable to each program

PMTA APPLICATIONS BY PRODUCT CATEGORY: STATUTORILY REGULATED PRODUCTS CUMULATIVE TOTAL

	Received	Open	Closed*				
			Marketing Granted	Marketing Denial	RTF	RTA	Withdrawn
Cigarettes	11	2	4	0	2	0	3
Roll Your Own	4	0	0	0	4	0	0
Smokeless	14	6	8	0	0	0	0
Total	29	8	21				

* Closed means CTP has taken an action on an application. Closed includes refuse-to-accept, refuse-to-file, withdrawn, closure due to administrative issues, environmental information request letter, predicate advice letter, removed from review, or issuance of order letter as applicable to each program

PMTA APPLICATIONS BY PRODUCT CATEGORY: DEEMED PRODUCTS

	Received FY 19	Open FY 19	Closed* FY 19				
			Marketing Granted	Marketing Denial	RTF	RTA	Withdrawn
Cigars	0	0	0	0	0	0	0
Pipe	0	0	0	0	0	0	0
Water Pipe	0	0	0	0	0	0	0
ENDS	16	15	0	0	0	1	0
Other	0	0	0	0	0	0	0
Total	16	15	1				

* Closed means CTP has taken an action on an application. Closed includes refuse-to-accept, refuse-to-file, withdrawn, closure due to administrative issues, environmental information request letter, predicate advice letter, removed from review, or issuance of order letter as applicable to each program

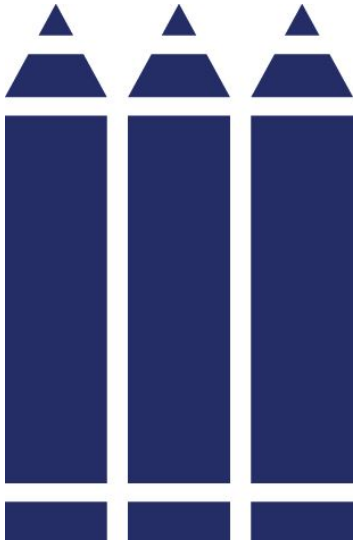
PMTA APPLICATIONS BY PRODUCT CATEGORY: DEEMED PRODUCTS CUMULATIVE TOTAL

	Received	Open	Closed*				
			Marketing Granted	Marketing Denial	RTF	RTA	Withdrawn
Cigars	0	0	0	0	0	0	0
Pipe	0	0	0	0	0	0	0
Water Pipe	1	0	0	0	1	0	0
ENDS	383	15	0	0	0	368	0
Other	4	4	0	0	0	0	0
Total	389	19	370				

* Closed means CTP has taken an action on an application. Closed includes refuse-to-accept, refuse-to-file, withdrawn, closure due to administrative issues, environmental information request letter, predicate advice letter, removed from review, or issuance of order letter as applicable to each program

SUMMARY OF KEY PMTA FEATURES

- Primary pathway to legally market a new tobacco product
- PMTA does not require a predicate tobacco product
  - Not a valid SE predicate
- PMTA may have postmarket reporting
- May be referred TPSAC
- Samples may be required (section 910(b)(1)(E))
- Action on a PMTA occurs within 180 days (section 910(c)(1)(A))

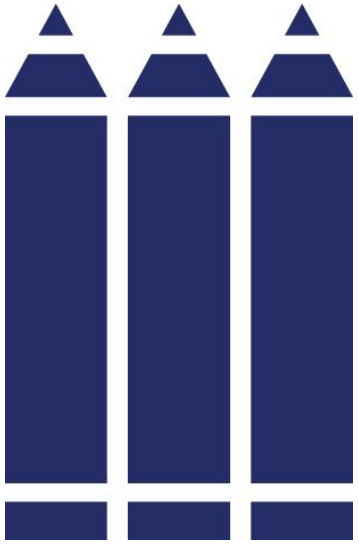


PMTA PROPOSED RULE

- FDA issued a proposed rule “Premarket Tobacco Product Applications and Recordkeeping Requirements” that would set forth requirements for premarket tobacco product applications (PMTAs) and would require manufacturers to maintain records establishing that their tobacco products are legally marketed. This proposed rule will also provide information as to how the agency intends to evaluate these submissions

- FDA published this proposed rule on September 25, 2019

- The comment period is open through November 25, 2019



See: https://www.federalregister.gov/documents/2019/09/25/2019-20315/premarket-tobacco-product-applications-and-recordkeeping-requirements

TAKE-HOME POINTS

- **Submission**
  - Grouping PMTA submissions
    - Applicant can include multiple tobacco products in one application
    - Clearly identify all tobacco products, providing unique identification for each product, and identifying which information is applicable to each product
  - Applications must contain all required elements for filing (e.g. submitting in portions may impact filing)
- **Review**
  - FDA will notify you if additional items are needed for review
  - FDA is not obligated to review unsolicited amendments
- **Action**
  - FDA will notify you by letter
  - Your letter will provide any postmarket reporting expectations, if applicable
- A proposed rule is available for comment

HELPFUL RESOURCES

- FDA/CTP PMTA webpage:
  - Premarket Tobacco Product Applications
  - Premarket Tobacco Product Marketing Orders
- Rules:
  - Refuse To Accept Procedures for Premarket Tobacco Product Submissions
  - Proposed rule for premarket tobacco product applications
- Memos:
  - Scientific Policy Memoranda about FDA Review of Tobacco Product Applications
- Guidance:
  - Final Guidance: Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS) (2019)
  - Final Guidance: Meetings with Industry and Investigators on the Research and Development of Tobacco Products (2016)
  - Draft Guidance: Applications for Premarket Review of New Tobacco Products (2011)
- Webinars:
  - Premarket Tobacco Product Applications (PMTA) for Electronic Nicotine Delivery System (ENDS)

THANK YOU