



# Pathways for Approval for Post-PMTA Product Modifications

October 25, 2019

**Matt Holman**, Director, Office of Science, CTP, FDA

**Patricia Miller**, Senior Director, Premarket Tobacco Applications, Altria Client Services LLC

*Moderated by* **Elizabeth Oestreich**, Vice President, Regulatory Compliance, Greenleaf Health

## AGENDA:

- Current state of modifications
- Why are we discussing this topic?
- Presentations
- Discussion on FDA's proposed rule and implementation
- Questions



## **New Tobacco Product**

Section 910(a)(1) of the FD&C Act defines a new tobacco product as:

- Any tobacco product (including those products in test markets) that was not commercially marketed in the US as of February 15, 2007 or
- Any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed after February 15, 2007.

# Premarket Tobacco Product Applications and Recordkeeping Requirements Proposed Rule – September 25, 2019

## Comment period closes on November 25, 2019



50566

Federal Register / Vol. 84, No. 186 / Wednesday, September 25, 2019 / Proposed Rules

### DEPARTMENT OF HEALTH AND HUMAN SERVICES

#### Food and Drug Administration

#### 21 CFR Parts 1100, 1107, and 1114

[Docket No. FDA-2019-N-2854]

RIN 0910-AH44

#### Premarket Tobacco Product Applications and Recordkeeping Requirements

**AGENCY:** Food and Drug Administration,  
HHS.

**ACTION:** Proposed rule.

**SUMMARY:** The Food and Drug Administration (FDA) is issuing a proposed rule 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. The proposed rule would help to ensure

#### Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a

with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.fda.gov/regulatory-information/dockets-management>.



# FDA'S CENTER FOR TOBACCO PRODUCTS: *PATHWAY FOR APPROVAL OF POST-PMTA PRODUCT MODIFICATIONS*

*Matthew R. Holman, Ph.D.  
Director  
Office of Science  
Center for Tobacco Products*

*Disclaimer: This is not a formal dissemination of information by FDA and does not represent Agency position or policy.*

# WHAT DOES THE PMTA RULE PROPOSE?

- Basic content and format
- General review procedures
  - From application receipt to order issuance
  - Communications from FDA
- Recordkeeping
  - Establishing that tobacco product is legally marketed
- Inspections

# WHAT DOES THE PMTA RULE PROPOSE?

- Electronic submission requirement
- Refuse To Accept (RTA) criteria
  - Must meet minimal content & format requirements
- Refuse To File (RTF) criteria
  - Must include substantive information on product health risks, comparative tobacco product information, abuse liability, actual use, likelihood of changes in use behavior by current users and non-users, & consumer perceptions

# WHAT ARE SOME BENEFITS OF THE PMTA RULE?

- Helps ensure that PMTAs contain sufficient information for FDA to determine whether to issue a marketing order
- Facilitates submission of streamlined PMTAs
  - Supplemental PMTA & Resubmission
  - Reduces burden on FDA & applicants
- Creates postmarket reporting requirements
  - Allows FDA & applicants to assess public health impact of product marketing



# WHAT ARE SOME BENEFITS OF THE PMTA RULE?

- Describes how to use scientific literature to bridge to new product
  - Data on products other than new product can be informative
- Clarifies the 180-day review period
  - Describes when FDA may pause or extend the review clock

## Proposed § 1114.15

“Applicants that *have received a marketing order* for a tobacco product may...submit a supplemental PMTA to seek marketing authorization for modifications to such product... Supplemental PMTAs must include *new information concerning modifications* that create the new tobacco product but allow the applicant to satisfy the remaining application requirements *by crossreferencing applicable content from the previously submitted PMTA* for the original tobacco product. Applicants may submit supplemental PMTAs *only for modifications that require the submission of limited new information.*”

## Potentially Appropriate for Supplemental PMTA

- Modification to meet product standard (if specified by FDA)
- Changes in connection type/thread size
- Minor software changes not affecting device functionality
- Minor changes in e-liquid volume, viscosity or boiling temperature
- Minor changes in draw resistance
- Minor changes in air flow rate
- Changes to coil configuration if number of coils, coil gauge, material, and overall coil resistance remain unchanged
- Changes to amount of wicking material
- Minor changes in wick ignition temperature

## Likely *Not* Appropriate for Supplemental PMTA

- Modification that might increase risk of harm to individual health from the product
- Modifications that may alter tobacco product use behavior and initiation, such as modifications that have strong youth appeal
- Design modifications that change the category or subcategory of the product (e.g., modifying a closed e-cigarette to be an open e-cigarette)

## Not Allowed for Supplemental PMTA

- Marketing order for the original tobacco product has been
  - Withdrawn
  - Temporarily suspended
  - Is subject of temporary suspension or withdrawal proceedings by FDA
- FDA may authorize exception to the situations above
  - Applicant must request exception
  - If reason for the temporary suspension or withdrawal is unrelated to sufficiency or reliability of information in the PMTA

# WHY IS CTP PROPOSING SUPPLEMENTAL PMTA?

- Reduces review burden on CTP
  - Not reassessing information that has already been evaluated
- Maintains rigorous standard for issuing marketing orders
  - Doesn't change legal or scientific requirements for order
- Consistent with other FDA Centers
  - Ex: NDA supplements

# WHY IS CTP PROPOSING SUPPLEMENTAL PMTA?

- Allows for faster marketplace changes that are positive for public health
  - Ex: Compliance with product standards
  - Ex: Safety improvements
- Allows applicant to avoid resubmitting information already provided to CTP
  - Doesn't slow down speed of positive marketplace changes
  - Provides information to CTP in most useful way

- Proposed rule provides public with CTP's thinking on PMTAs
  - Read it carefully
  - Preamble outlines why we are proposing what is captured in codified
- Supplemental PMTAs are important creation
  - Allows focusing of resources are most salient information
- All stakeholders should provide comments to the proposed rule by November 25
  - CTP evaluates all comments in preparing the final rule





# Pathways for Approval of Post- PMTA Modifications

Patricia M. Miller, Esq.  
Senior Director, Regulatory Affairs  
Altria Client Services



# Importance of Modifications – Technology Changes Rapidly

2009



2019



# Potential Drivers of Product Modifications

**Consumer Complaints**

**Product Safety Concerns**

**Product Misuse**

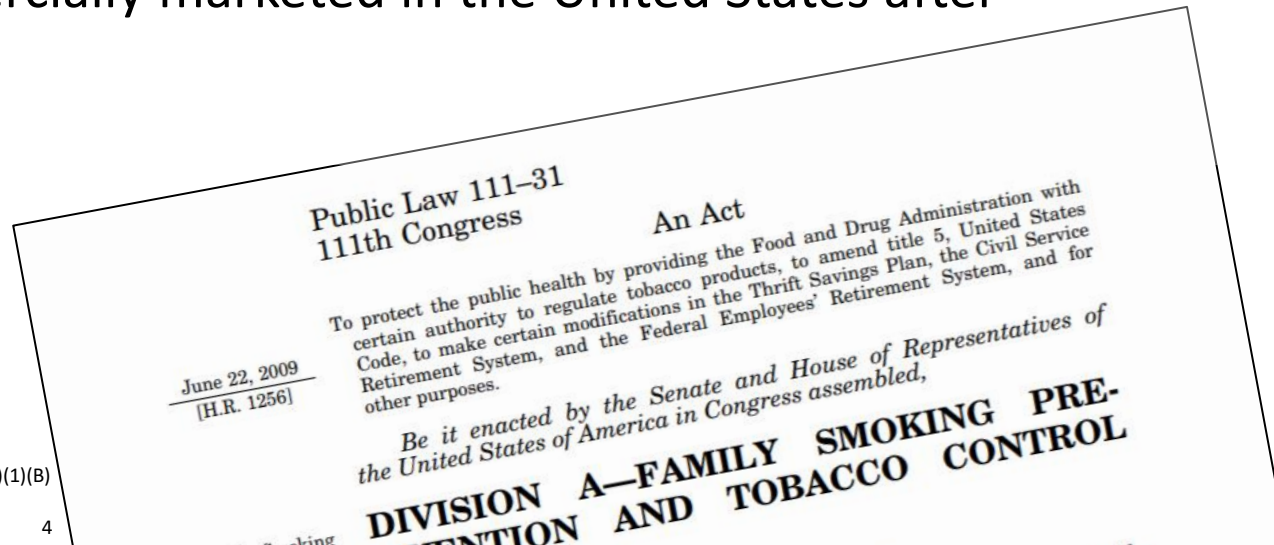
**Technology to Prevent Youth Access**

**Supplier Issues**

**Manufacturing Efficiencies**

# Modifications Can Create a “New” Product

**New Tobacco Product** means...any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007.



Tobacco Control Act § 910(a)(1)(B); 21 USC § 387j(a)(1)(B)

# Current Product Change Pathways

## Substantial Equivalence:

- Requires predicate product
- Same characteristics, or different characteristics but product does not raise different questions of public health

## SE Exemption:

- Legally marketed product
- Modified by adding or deleting a tobacco additive, or increasing or decreasing the quantity of an existing tobacco additive
- Minor modification

# Current Product Change Pathways

## PMTA Marketing Orders

- Limited post-authorization changes implied by periodic reporting:
  - Changes to manufacturing process, facilities, or controls (*that do not result in product modification*)
  - Final printed labeling, with description of all changes

FDA NEWS RELEASE

**FDA permits sale of IQOS Tobacco Heating System through premarket tobacco product application pathway**

*Agency places stringent marketing restrictions on heated tobacco products aimed at preventing youth access and exposure to the new products*

**For Immediate Release:**

April 30, 2019

# Proposed Supplemental PMTA – Overview

- Alternative PMTA format to reduce the burden associated with submission and review
- “Submission of limited information or revisions to the PMTA to make it apply to the modified tobacco product.”<sup>1</sup>
- Can be used to comply with a product standard under § 907
- Format/content – 1) New content sections; 2) Cross-referenced content sections
- Certification of no other modifications

1. Premarket Tobacco Product Applications and Recordkeeping Requirements Proposed Rule, September 2019

The diagram illustrates the flow from a PMTA Cover Sheet to a PMTA Cover Sheet with a Technical Project Lead Review (TPL) table. Four blue arrows point from the top PMTA Cover Sheet to the bottom PMTA Cover Sheet, indicating the transition from a standard PMTA to one with a TPL review.

**Top PMTA Cover Sheet:**

U.S. FOOD & DRUG  
DEPARTMENT OF HEALTH & HUMAN SERVICES

PMTA Cover Sheet: Technical Project Lead Review (TPL)

Information for Submission	
Applicant	Philip Morris Products U.S.
Product Monograph	Philip Morris Products U.S.
Submission Date	01-15-2017
PLM Receipt Date	01-15-2017

Primary PMTA	Cross-referenced PMTA	Primary PMTA
PM000001	PM000002	PM000003
PM000004	PM000005	PM000006
PM000007	PM000008	PM000009
PM000010	PM000011	PM000012
PM000013	PM000014	PM000015
PM000016	PM000017	PM000018
PM000019	PM000020	PM000021
PM000022	PM000023	PM000024
PM000025	PM000026	PM000027
PM000028	PM000029	PM000030
PM000031	PM000032	PM000033
PM000034	PM000035	PM000036
PM000037	PM000038	PM000039
PM000040	PM000041	PM000042
PM000043	PM000044	PM000045
PM000046	PM000047	PM000048
PM000049	PM000050	PM000051
PM000052	PM000053	PM000054
PM000055	PM000056	PM000057
PM000058	PM000059	PM000060
PM000061	PM000062	PM000063
PM000064	PM000065	PM000066
PM000067	PM000068	PM000069
PM000070	PM000071	PM000072
PM000073	PM000074	PM000075
PM000076	PM000077	PM000078
PM000079	PM000080	PM000081
PM000082	PM000083	PM000084
PM000085	PM000086	PM000087
PM000088	PM000089	PM000090
PM000091	PM000092	PM000093
PM000094	PM000095	PM000096
PM000097	PM000098	PM000099
PM000100	PM000101	PM000102
PM000103	PM000104	PM000105
PM000106	PM000107	PM000108
PM000109	PM000110	PM000111
PM000112	PM000113	PM000114
PM000115	PM000116	PM000117
PM000118	PM000119	PM000120
PM000121	PM000122	PM000123
PM000124	PM000125	PM000126
PM000127	PM000128	PM000129
PM000130	PM000131	PM000132
PM000133	PM000134	PM000135
PM000136	PM000137	PM000138
PM000139	PM000140	PM000141
PM000142	PM000143	PM000144
PM000145	PM000146	PM000147
PM000148	PM000149	PM000150
PM000151	PM000152	PM000153
PM000154	PM000155	PM000156
PM000157	PM000158	PM000159
PM000160	PM000161	PM000162
PM000163	PM000164	PM000165
PM000166	PM000167	PM000168
PM000169	PM000170	PM000171
PM000172	PM000173	PM000174
PM000175	PM000176	PM000177
PM000178	PM000179	PM000180
PM000181	PM000182	PM000183
PM000184	PM000185	PM000186
PM000187	PM000188	PM000189
PM000190	PM000191	PM000192
PM000193	PM000194	PM000195
PM000196	PM000197	PM000198
PM000199	PM000200	PM000201
PM000202	PM000203	PM000204
PM000205	PM000206	PM000207
PM000208	PM000209	PM000210
PM000211	PM000212	PM000213
PM000214	PM000215	PM000216
PM000217	PM000218	PM000219
PM000220	PM000221	PM000222
PM000223	PM000224	PM000225
PM000226	PM000227	PM000228
PM000229	PM000230	PM000231
PM000232	PM000233	PM000234
PM000235	PM000236	PM000237
PM000238	PM000239	PM000240
PM000241	PM000242	PM000243
PM000244	PM000245	PM000246
PM000247	PM000248	PM000249
PM000250	PM000251	PM000252
PM000253	PM000254	PM000255
PM000256	PM000257	PM000258
PM000259	PM000260	PM000261
PM000262	PM000263	PM000264
PM000265	PM000266	PM000267
PM000268	PM000269	PM000270
PM000271	PM000272	PM000273
PM000274	PM000275	PM000276
PM000277	PM000278	PM000279
PM000280	PM000281	PM000282
PM000283	PM000284	PM000285
PM000286	PM000287	PM000288
PM000289	PM000290	PM000291
PM000292	PM000293	PM000294
PM000295	PM000296	PM000297
PM000298	PM000299	PM000300
PM000301	PM000302	PM000303
PM000304	PM000305	PM000306
PM000307	PM000308	PM000309
PM000310	PM000311	PM000312
PM000313	PM000314	PM000315
PM000316	PM000317	PM000318
PM000319	PM000320	PM000321
PM000322	PM000323	PM000324
PM000325	PM000326	PM000327
PM000328	PM000329	PM000330
PM000331	PM000332	PM000333
PM000334	PM000335	PM000336
PM000337	PM000338	PM000339
PM000340	PM000341	PM000342
PM000343	PM000344	PM000345
PM000346	PM000347	PM000348
PM000349	PM000350	PM000351
PM000352	PM000353	PM000354
PM000355	PM000356	PM000357
PM000358	PM000359	PM000360
PM000361	PM000362	PM000363
PM000364	PM000365	PM000366
PM000367	PM000368	PM000369
PM000370	PM000371	PM000372
PM000373	PM000374	PM000375
PM000376	PM000377	PM000378
PM000379	PM000380	PM000381
PM000382	PM000383	PM000384
PM000385	PM000386	PM000387
PM000388	PM000389	PM000390
PM000391	PM000392	PM000393
PM000394	PM000395	PM000396
PM000397	PM000398	PM000399
PM000400	PM000401	PM000402
PM000403	PM000404	PM000405
PM000406	PM000407	PM000408
PM000409	PM000410	PM000411
PM000412	PM000413	PM000414
PM000415	PM000416	PM000417
PM000418	PM000419	PM000420
PM000421	PM000422	PM000423
PM000424	PM000425	PM000426
PM000427	PM000428	PM000429
PM000430	PM000431	PM000432
PM000433	PM000434	PM000435
PM000436	PM000437	PM000438
PM000439	PM000440	PM000441
PM000442	PM000443	PM000444
PM000445	PM000446	PM000447
PM000448	PM000449	PM000450
PM000451	PM000452	PM000453
PM000454	PM000455	PM000456
PM000457	PM000458	PM000459
PM000460	PM000461	PM000462
PM000463	PM000464	PM000465
PM000466	PM000467	PM000468
PM000469	PM000470	PM000471
PM000472	PM000473	PM000474
PM000475	PM000476	PM000477
PM000478	PM000479	PM000480
PM000481	PM000482	PM000483
PM000484	PM000485	PM000486
PM000487	PM000488	PM000489
PM000490	PM000491	PM000492
PM000493	PM000494	PM000495
PM000496	PM000497	PM000498
PM000499	PM000500	PM000501
PM000502	PM000503	PM000504
PM000505	PM000506	PM000507
PM000508	PM000509	PM000510
PM000511	PM000512	PM000513
PM000514	PM000515	PM000516
PM000517	PM000518	PM000519
PM000520	PM000521	PM000522
PM000523	PM000524	PM000525
PM000526	PM000527	PM000528
PM000529	PM000530	PM000531
PM000532	PM000533	PM000534
PM000535	PM000536	PM000537
PM000538	PM000539	PM000540
PM000541	PM000542	PM000543
PM000544	PM000545	PM000546
PM000547	PM000548	PM000549
PM000550	PM000551	PM000552
PM000553	PM000554	PM000555
PM000556	PM000557	PM000558
PM000559	PM000560	PM000561
PM000562	PM000563	PM000564
PM000565	PM000566	PM000567
PM000568	PM000569	PM000570
PM000571	PM000572	PM000573
PM000574	PM000575	PM000576
PM000577	PM000578	PM000579
PM000580	PM000581	PM000582
PM000583	PM000584	PM000585
PM000586	PM000587	PM000588
PM000589	PM000590	PM000591
PM000592	PM000593	PM000594
PM000595	PM000596	PM000597
PM000598	PM000599	PM000600
PM000601	PM000602	PM000603
PM000604	PM000605	PM000606
PM000607	PM000608	PM000609
PM000610	PM000611	PM000612
PM000613	PM000614	PM000615
PM000616	PM000617	PM000618
PM000619	PM000620	PM000621
PM000622	PM000623	PM000624
PM000625	PM000626	PM000627
PM000628	PM000629	PM000630
PM000631	PM000632	PM000633
PM000634	PM000635	PM000636
PM000637	PM000638	PM000639
PM000640	PM000641	PM000642
PM000643	PM000644	PM000645
PM000646	PM000647	PM000648
PM000649	PM000650	PM000651
PM000652	PM000653	PM000654
PM000655	PM000656	PM000657
PM000658	PM000659	PM000660
PM000661	PM000662	PM000663
PM000664	PM000665	PM000666
PM000667	PM000668	PM000669
PM000670	PM000671	PM000672
PM000673	PM000674	PM000675
PM000676	PM000677	PM000678
PM000679	PM000680	PM000681
PM000682	PM000683	PM000684
PM000685	PM000686	PM000687
PM000688	PM000689	PM000690
PM000691	PM000692	PM000693
PM000694	PM000695	PM000696
PM000697	PM000698	PM000699
PM000700	PM000701	PM000702
PM000703	PM000704	PM000705
PM000706	PM000707	PM000708
PM000709	PM000710	PM000711
PM000712	PM000713	PM000714
PM000715	PM000716	PM000717
PM000718	PM000719	PM000720
PM000721	PM000722	PM000723
PM000724	PM000725	PM000726
PM000727	PM000728	PM000729
PM000730	PM000731	PM000732
PM000733	PM000734	PM000735
PM000736	PM000737	PM000738
PM000739	PM000740	PM000741
PM000742	PM000743	PM000744
PM000745	PM000746	PM000747
PM000748	PM000749	PM000750
PM000751	PM000752	PM000753
PM000754	PM000755	PM000756
PM000757	PM000758	PM000759
PM000760	PM000761	PM000762
PM000763	PM000764	PM000765

# Proposed Supplemental PMTA Assessment

## Proposed Supplemental PMTA Strengths

- Creation of streamlined pathway
- Builds from § 910 framework
- Clear guidance on proposed content
- Helpful examples of modifications – for ENDS, at least

---

### Potentially Appropriate for Supplemental PMTA Format

---

- Changes in connection type/thread size (*e.g.*, 510).
- Minor Software Changes not affecting device functionality.
  - Changes to user interface.
  - Changes in recording/data capture properties.
- Minor changes in e-liquid volume, viscosity or boiling temperature.
- Minor changes in draw resistance.
- Minor changes in air flow rate.
- Changes to coil configuration if number of coils, coil gauge, material, and overall coil resistance remain unchanged.
- Changes to amount of wicking material.
- Minor changes in wick ignition temperature.

---

### Likely Not Appropriate for Supplemental PMTA Format

---

- Any modification that might increase risk of harm to individual health from the product.
- Modifications that may alter tobacco product use behavior and initiation, such as modifications that have strong youth appeal.
- Design modifications that change the category or subcategory of the product (*e.g.*, modifying a closed e-cigarette to be an open e-cigarette).



# Proposed Supplemental PMTA Assessment

## Ambiguity of Supplemental Pathway Access

“...only for a modification or modifications that require the submission of limited information...”

“applicant would not be able to submit...to the extent that reviewing a supplemental application would be...confusing, cumbersome, or otherwise inefficient...”

“Changes that require multiple, sweeping, or difficult-to-trace changes...would be more efficient to review in full text format...”

*Premarket Tobacco Product Applications and Recordkeeping Requirements Proposed Rule, September 2019 (Emphasis added)*

# Proposed Supplemental PMTA Assessment

## Length of Review Period

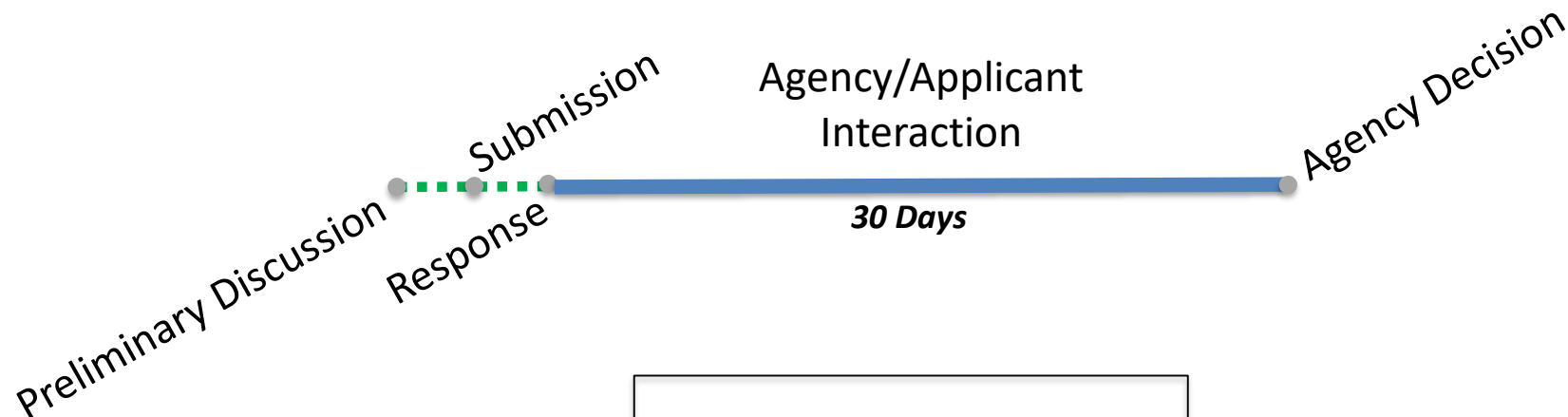
- Length of supplemental PMTA review process not specified in Proposed Rule or preamble
- PMTA = 180-day review period?
- But – “FDA estimates further that a supplemental PMTA will take 25 percent of the time it takes to do an original submission...”<sup>1</sup>

1. *Premarket Tobacco Product Applications and Recordkeeping Requirements Proposed Rule, September 2019*

# PMTA Timeline



# Possible Review for Minor Modifications



- Minor modifications
- Interaction with FDA
- Abbreviated timeline