MODIFIED RISK TOBACCO PRODUCT APPLICATION (MRTPA) REVIEW PROCESS

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AGENDA

- Statutory Requirements
- Review Process
  - Pre meeting
  - Acceptance
  - Filing
  - Review
  - Postmarket

  Surveillance and Studies

- Metrics
- Key Features
- Helpful Resources

STATUTORY REQUIREMENTS, SECTION 911

STATUTORY REQUIREMENTS

Section 911(b)(1) defines Modified Risk Tobacco Products (MRTPs):

Tobacco products sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products; this includes products whose label, labeling or advertising represents (explicitly or implicitly) that:

- The product presents a lower risk of tobacco-related disease or is less harmful than other commercially marketed tobacco products
- The product or its smoke contains a reduced level of or presents a reduced exposure to a substance; or does not contain/is free of a substance

STATUTORY REQUIREMENTS

- **A tobacco product is also considered a Modified Risk Tobacco Product if:**
  - The descriptors “light”, “mild,” “low” or similar descriptors are used in its label, labeling or advertising; or
  - Its manufacturer has taken any action after June 22, 2009 directed to consumers through the media or otherwise, other than by means of label, labeling or advertising, that would be reasonably expected to result in consumers believing that the tobacco product may present a reduced risk of harm, tobacco-related disease, or exposure to a substance than commercially marketed tobacco products

STATUTORY REQUIREMENTS

- **In order for a Modified Risk Tobacco Product to be legally introduced or delivered for introduction into interstate commerce:**
  - Obtained marketing authorization from FDA; and
  - FDA must issue a Modified Risk Order (MRO) in line with FD&C Act, section 911(g).

MRTPA REVIEW PROCESS

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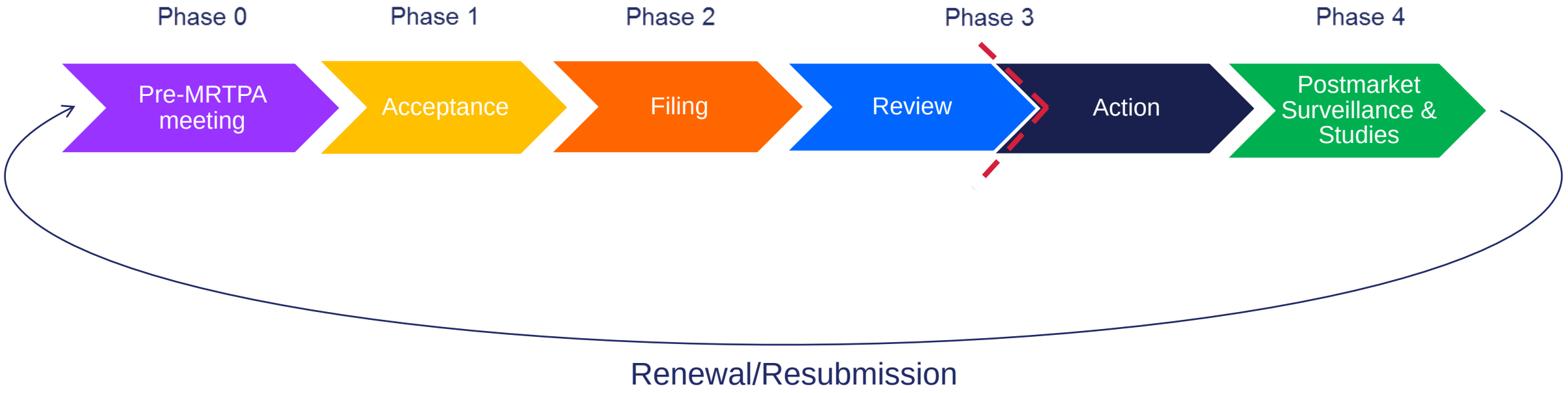

PRE-MRTPA MEETING (PHASE 0)

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

Pre-meetings can be help applicant gain information about:

- Samples
- End points
- Filing requirements
- Inspections: clinical and manufacturing
- Format of application for submission

Guidance - Meetings with Industry and Investigators on the Research and Development of Tobacco Products (Revised July 2016)

Pre meeting

ACCEPTANCE (PHASE 1)

- Ensure the product falls under CTP jurisdiction
- Confirm the regulatory requirements of an application are included in submission
- Expected outcome:
  - Accepted and Acknowledged

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

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

Acceptance

FILING (PHASE 2) (continued)

In order to File the MRTPA, it must contain the following (as outlined in 911(d)):

1. a description of the proposed product and any proposed advertising and labeling
2. the conditions for using the product
3. the formulation of the product
4. sample product labels and labeling
5. all documents (including underlying scientific information) relating to research findings conducted, supported, or possessed by the tobacco product manufacturer relating to the effect of the product on tobacco-related diseases and health-related conditions, including information both favorable and unfavorable to the ability of the product to reduce risk or exposure and relating to human health
6. data and information on how consumers actually use the tobacco product
7. such other information as the Secretary may require

Filing

FILING (PHASE 2) (continued)

- Expected outcome:
  - Application filed

    or
  - Refuse to File

Filing

SUBSTANTIVE REVIEW (PHASE 3)

- Application publicly posted on FDA website
- Multi-disciplinary approach to determine if the modified risk claim can be substantiated
- Sample testing may be conducted
- Conduct inspections, as needed
  - Clinical/Nonclinical
  - Manufacturing
- Tobacco Products Scientific Advisory Committee (TPSAC) publically provides recommendations to FDA

Review

ACTION (PHASE 3)

Action Results in:

Modified Risk Order

or

Denial

or

Response Letter

Action

POSTMARKET SURVEILLANCE & STUDIES (PHASE 4)

- Postmarket surveillance and studies requirements are outlined within the modified risk order
  - The applicant submits a postmarket surveillance protocol to FDA
  - FDA reviews the applicant's proposed protocol and determines whether to approve the protocol
  - FDA monitors and reviews data submitted as part of postmarket surveillance

Postmarket

RENEWAL/RESUBMISSION

- The FD&C Act limits authorized modified risk order claims to a term specified in the modified risk order
  - The applicant can renew a modified risk order claim
  - The applicant can also choose to edit the claim based on new information found during the postmarket surveillance and studies, and seek renewal of the MRTPA, referencing the previous application and noting any changes

WITHDRAWAL OF AN APPLICATION

- Applicants may withdraw an application at any time.
  - If a withdrawal is requested, FDA issues a letter acknowledging the withdrawal request
  - The process ends at withdrawal, no matter what phase the application is in

KEY FEATURES, METRICS, AND RESOURCES

KEY FEATURES OF MODIFIED RISK APPLICATIONS AND ORDERS

FDA

FDA:

- must make MRTPAs (except personal privacy, trade secrets or otherwise confidential commercial information) available for public comment.
- must refer MRTPAs to the TPSAC for recommendations.
- intends to make decision on the MRTPA within 360 days.

Modified risk orders are:

- issued for **individual products,** not for a class of tobacco products.
- are valid for a duration specified by FDA. An applicant may request renewal of the order.

MRTPA METRICS

	# of applications (through September 2018)
Received	37
Acknowledged	26
RTA	10
Filed	20
RTF	4
Withdrawn	5
Response	8

*In addition to applications having been withdrawn, applications at various stages in the review process, therefore these numbers may not necessarily total to 100%

HELPFUL RESOURCES

- FDA/CTP MRTP webpage:
  - https://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm304465.htm
- Rules:
  - Refuse To Accept Procedures for Premarket Tobacco Product Submissions
- Guidances:
  - Draft Guidance: Modified Risk Tobacco Product Applications (March 2012)
  - Final Guidance: Meetings with Industry and Investigators on the Research and Development of Tobacco Products (July 2016)
- Q & A: Modified Risk Tobacco Products:
  - https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm410712.htm