Modified Risk Tobacco Product Applications: Status Update

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Moderated by **J. Benneville (Ben) Haas**, Partner, Latham & Watkins LLP

Modified Risk Tobacco Product Applications: Status Update

J. Benneville (Ben) Haas, Partner,
Latham & Watkins LLP

Lessons Learned from MRTP Experiences

Jim Solyst

Swedish Match

Status of General Snus MRTPA

- First submitted in June 2014
  - Claims
- TPSAC meeting April 2015
- Evidence also used as the basis for a PMTA that was awarded in November 2015
- December 2016 Partial Decision
  - Message
  - Encouragement to continue the process
- Amendment submitted September 2018
- TPSAC February 2019
- Docket closes May 13, 2019

Lessons Learned: Interacting with CTP

- Act states the process is driven by the applicant not CTP: CTP does issue guidance; but it is up to the applicant to determine what evidence to submit.
- Pre- application submission meetings are essential and beneficial
- The hour- long meetings are useful but most important is the written responses from CTP
- But success of the meeting depends on the applicant providing questions written in a manner that provides information and can be answered, at least in part.

Evolving Understanding

- Exchanges between CTP and the applicant become more productive as documents – response letters, meeting summaries, decision documents—are issued.
- For example, the MRTPA meetings Swedish Match has had with CTP since 2017 have been more productive because there are documents to cite.

Evolution of the TPSAC

- The chair is vital to the success of an advisory committee.
  - Dr. John Samet –TPSAC Chair from 2009 to early 2015- was a "professional chair" who had chaired scores of advisory committees.
  - Current TPSAC Chair Dr. Robin Mermelstein did an excellent job at the most recent TPSAC meeting.
- There is value in having a committee with diverse but applicable scientific backgrounds, but the ideal committee member who someone who has extensive experience, particularly published articles—in nicotine science.
- The discussion is more valuable than the votes.

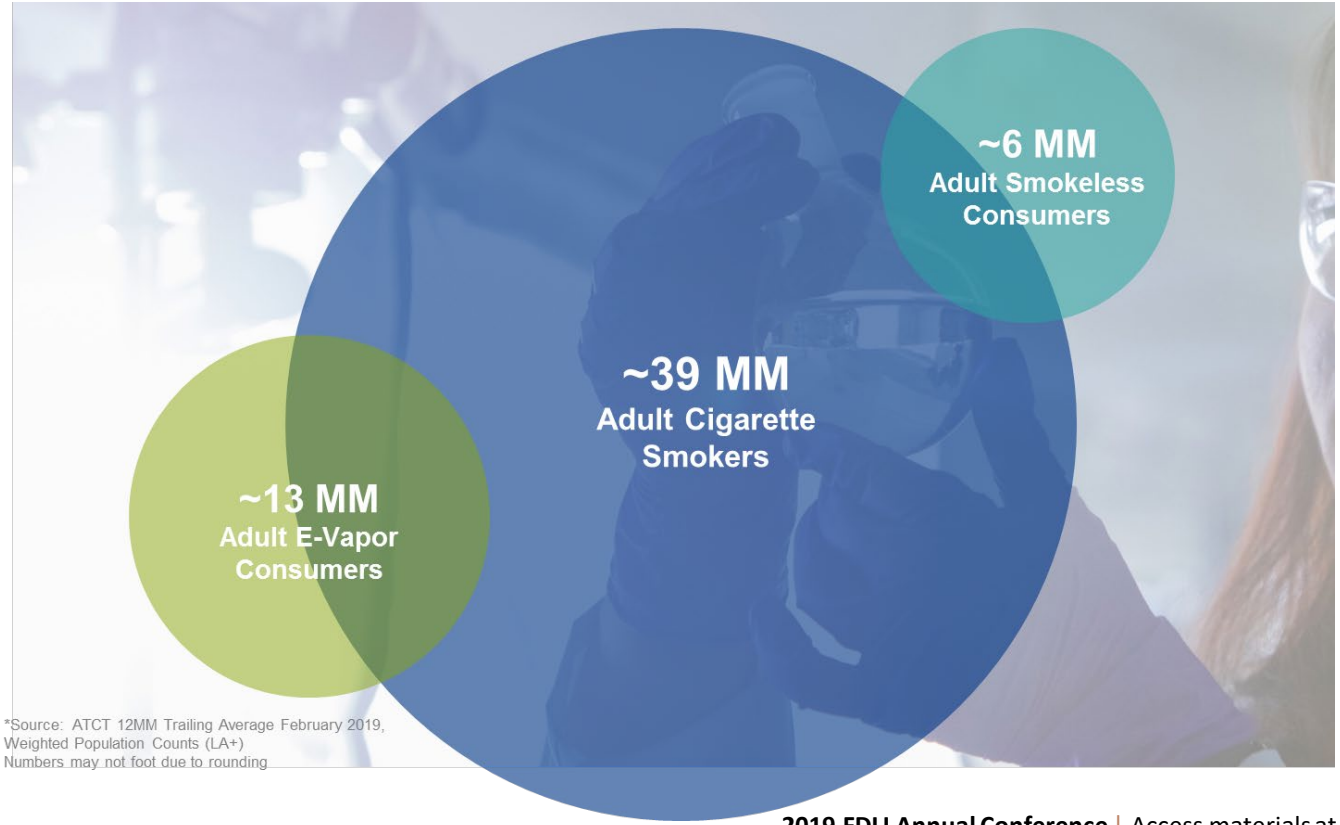
Preparing for a TPSAC Meeting

- Applicant Briefing Document
- FDA Briefing Document
- Comments to the Docket

Altria's Modified Risk Tobacco Product Application for Copenhagen Fine Cut Snuff

Michael Fisher, PhD
Altria Client Services, Regulatory Affairs
May 2, 2019

Harm Reduction Opportunities



*Source: ATCT 12MM Trailing Average February 2019, Weighted Population Counts (LA+)
Numbers may not foot due to rounding

Range of Potentially Lower Risk Products

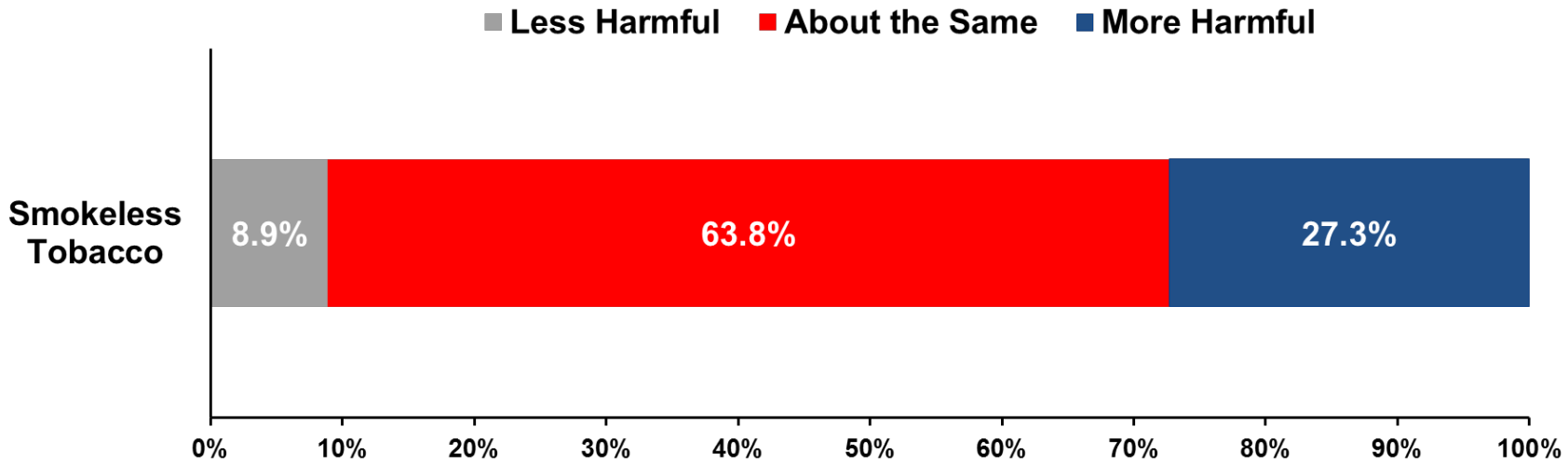
E-Vapor

Heat-not-Burn

Smokeless

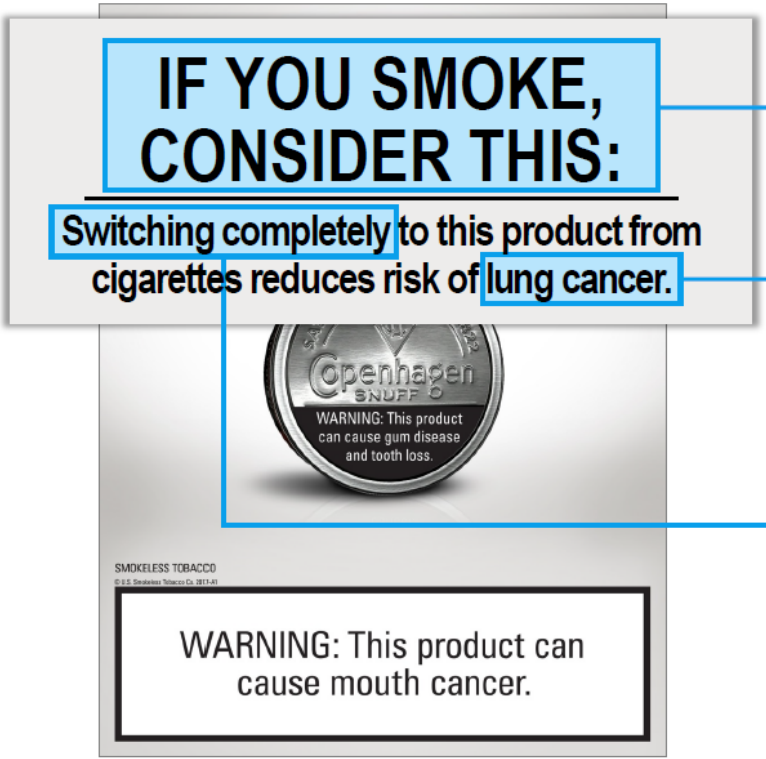
Note: Third party trademarks are the property of their respective owners and are included for informational purposes only.

Current Risk Perceptions



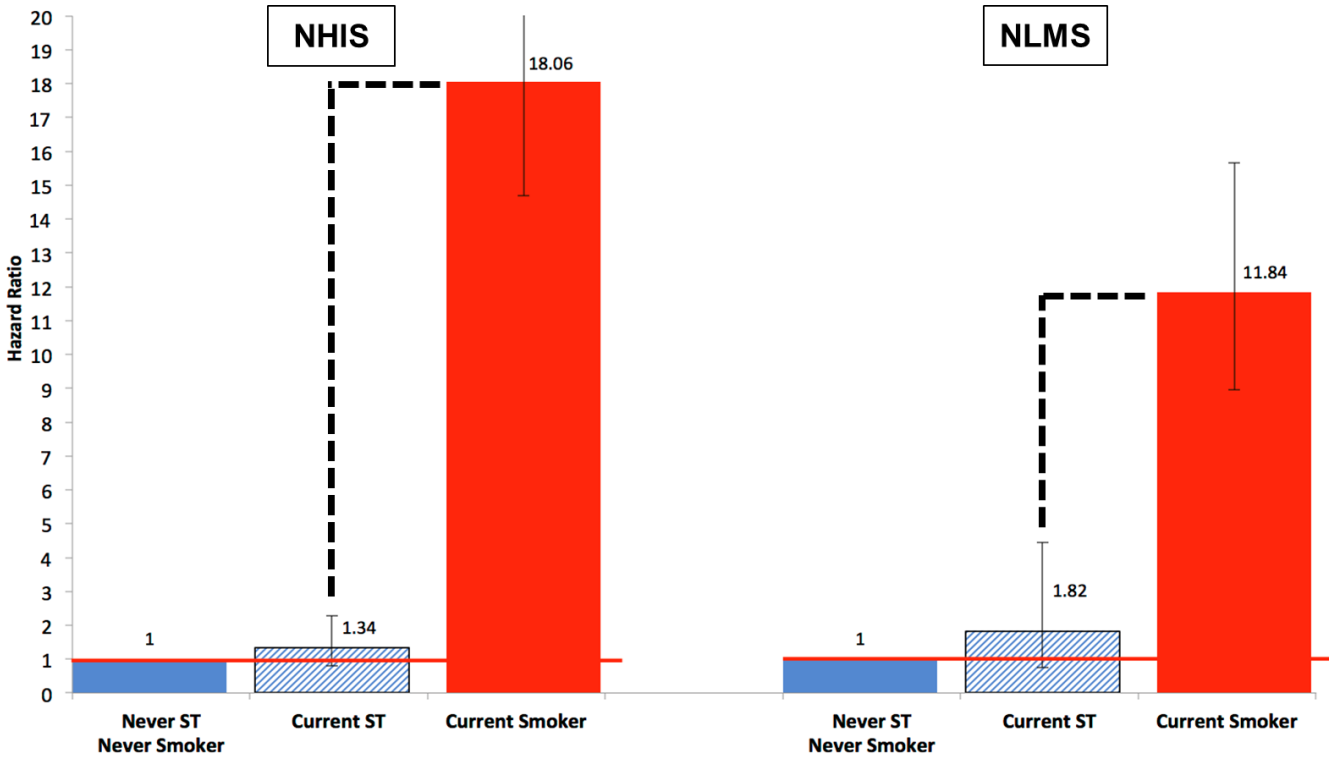
- *More than 90%* in FDA's PATH survey say that smokeless tobacco products are just *as harmful* or *more harmful* than cigarettes

Proposed Modified Risk Claim



1. **Draws the attention of adult smokers**
2. **Single disease focus**
   Neither states nor implies that the product presents no risk of lung cancer or other disease
3. **Desired single use behavior**

Lung Cancer Mortality Risks



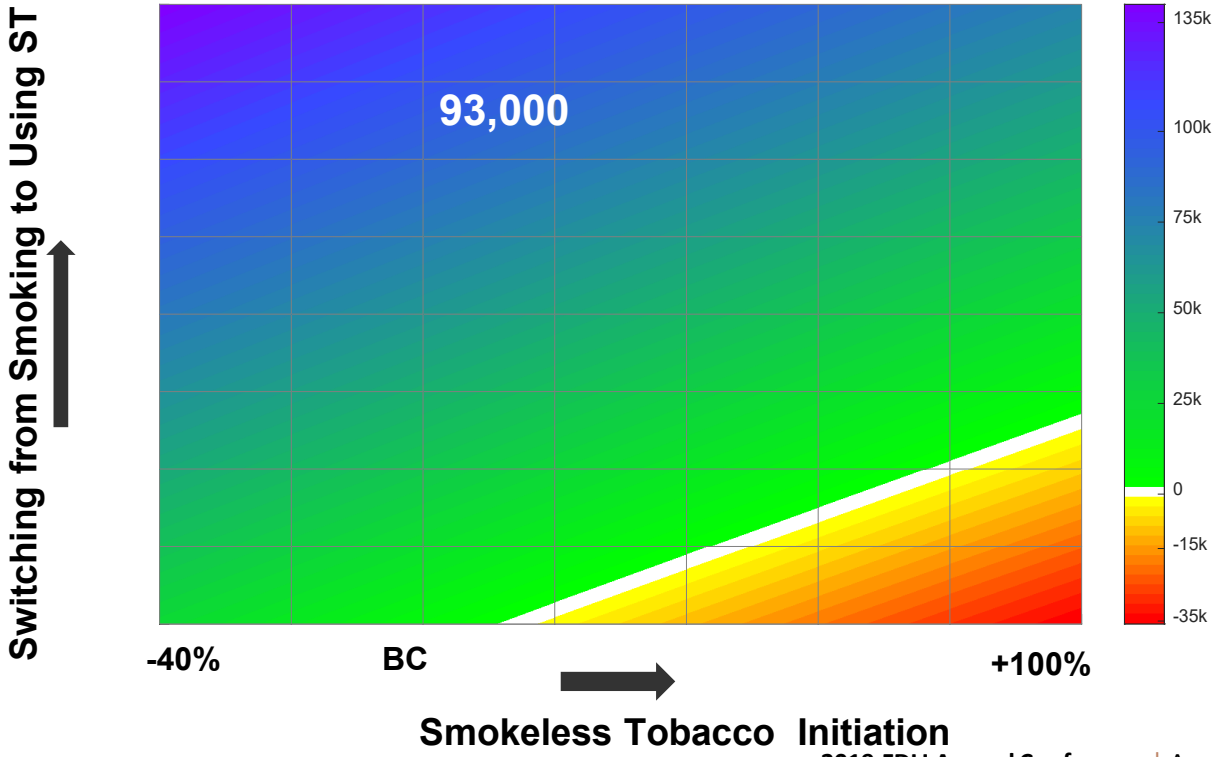
FDA & TPSAC Conclusions on Health Risk

- FDA: “Based on the evidence described above, the proposed modified risk claim “IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer” appears to be scientifically accurate.” – FDA Briefing Document, p. 21

- TPSAC: DISCUSS the available scientific evidence and VOTE on the whether the proposed modified risk claim is scientifically accurate (yes/no/abstain).

Yes	8
No	0
Abstain	1

Estimated Population Impact of Proposed Modified Risk Claim

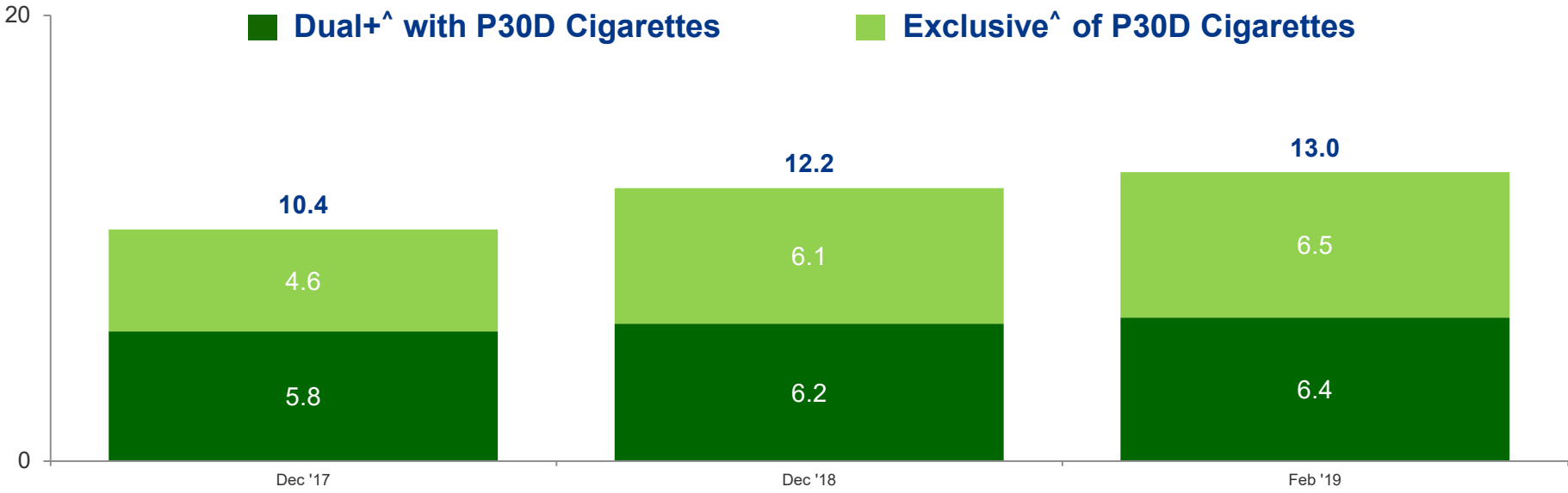


FDA Conclusion on Population Health Benefit

- FDA: “Computational modeling estimated a relatively small net population health benefit from market authorization of Copenhagen Snuff Fine Cut with the proposed modified risk claim.” FDA TPSAC presentation slide 49.

Changing E-vapor Use Patterns

12MM, By Usage - Total, in millions



*LA+, P30D Source: ATCT

Numbers may not foot due to rounding. 'N' represents weighted counts

FDA and Modified Risk Products

Key Public Health Issues

Dennis Henigan
Campaign for Tobacco-Free Kids

FDLI

March of the Modified Risk Products

- **PMI modified risk application for iQOS heated product**
  - "Switching completely from cigarettes to the iQOS system can reduce the risks of tobacco-related disease."
- **Camel snus modified risk application**
  - "Smokers who SWITCH COMPLETELY FROM CIGARETTES TO Camel SNUS can greatly reduce their risk of lung cancer, oral cancer, respiratory disease and heart disease."
- **US Smokeless Tobacco Company (Altria subsidiary) – modified risk application for Copenhagen moist snuff**
  - "IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer."
- **Amended Swedish Match modified risk application for Swedish snus**
  - "Using General Snus instead of cigarettes puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis."

FDLI

Section 911

- Purpose not to ensure easy pathway to market for reduced risk products.

- Companies must meet rigorous criteria
  - Product, *as actually used by consumers,*
    - Will reduce risk of harm to individual users
    - Will benefit population as a whole, taking into account tobacco product users and non-users

FDLI

Absence of Youth Perception Data

- Applications contain no data on youth perception of proposed modified risk messages.
- FDA's 2012 Draft Guidance on modified risk applications recommends consumer perception studies, including assessment of likelihood that youth will initiate use of product.
- In light of Draft Guidance, why have youth perception studies not be performed?

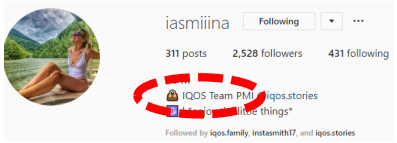
FDLI

Modified Risk Messages Not Limited to Adult Smokers

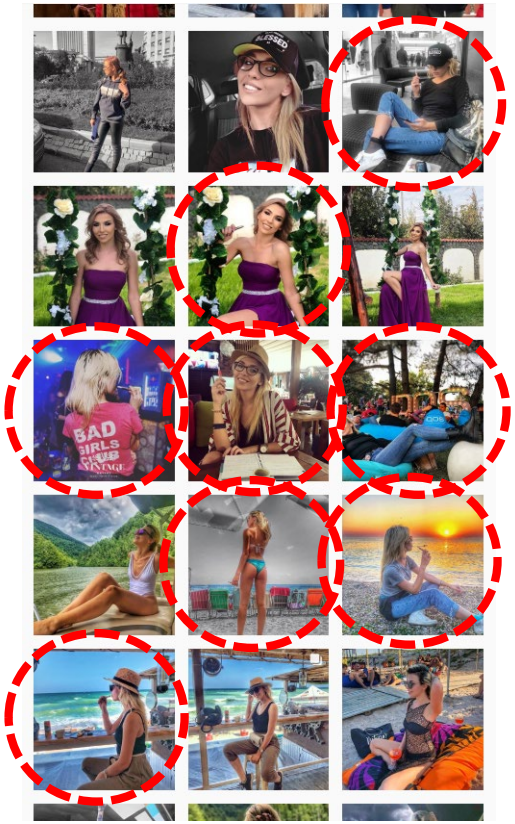
- Applicants' marketing plans do not direct messages only at adult smokers.
- Marketing plans include print ads, point of sale ads, social media.
- None of marketing plans limited to current smokers.
- IQOS: global marketing belies claim that US marketing will avoid youth and nonsmokers.

FDLI

Youthful Images by an IQOS Brand Ambassador



https://www.instagram.com/iasmiiina/



Will Smokers Actually Switch?

- In all four applications, evidence weak that smokers would switch completely to modified risk products.
- For smokeless products, U.S. experience far different than Sweden's.
- On IQOS, TPSAC skeptical that smokers would switch.

FDLI

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FDLI

MODIFIED RISK TOBACCO PRODUCT APPLICATIONS (MRTPAs)

Presented by:
Matthew R. Holman, PhD
Director, Office of Science
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U.S. Food and Drug Administration

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

RISK MODIFICATION ORDER STANDARD - 911(g)(1)

The FD&C Act requires FDA to determine if a proposed modified risk tobacco product (MRTP), as it is actually used by consumers, will:

(1) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and

(2) benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products

EXPOSURE MODIFICATION ORDER STANDARD - 911(G)(2)

For products that cannot receive an order under 911(g)(1), FDA may issue an order under 911(g)(2) if it determines that the applicant has demonstrated that, among other things:

- it is appropriate to promote the public health;
- the label, labeling, and advertising is limited to a claim that the product does not contain or is free of a substance or contains a reduced level or presents a reduced exposure;
- scientific evidence is not available, and cannot be made available without conducting long-term epidemiological studies, for an application to meet the standard for a 911(g)(1) order;
- scientific evidence that is available demonstrates that a substantial reduction in morbidity or mortality is reasonably likely; and
- testing shows that consumers will not be misled into believing that the product has been demonstrated to be less harmful or present less risk.

QUESTIONS RELEVANT TO THE MRTP EVALUATION

These questions are relevant to the evaluation of whether the applicant has met the applicable 911 standard:

1. Is there adequate scientific substantiation of the proposed modified risk information?
2. What are the health risks of the MRTP to individual tobacco users?
3. How do consumers perceive and understand the modified risk information?
4. What are the potential benefits and harms to the health of the population as a whole?

FDA PREMARKET SCIENTIFIC REVIEW OF MRTPAs

- Scientific review includes the following key areas of focus:
  - Identification of modified risk information
  - Substantiation of modified risk information
  - Relative health risks to individuals
  - Consumer understanding and perception
  - Impact to the population as a whole
  - Product description and characterization
  - Environmental review and NEPA

- Reviews are based on all available scientific evidence related the product(s) — both the information provided by the applicant, as well as any other relevant information available to the Agency, including from the general scientific literature.

WEIGHING THE EVIDENCE

- Evaluation of the evidence requires an assessment of the impact of a marketing authorization on both the individual, as well as the population as a whole. Elements include…
  - Effect of modified risk information on tobacco use behaviors (e.g., complete switching, dual use) of particular tobacco user groups (e.g., current smokers, youth)
  - Toxicity of the product
  - Changes in health risks based on tobacco use behaviors and toxicity of the product
- MRTP marketing order issued when the evidence supports a public health benefit

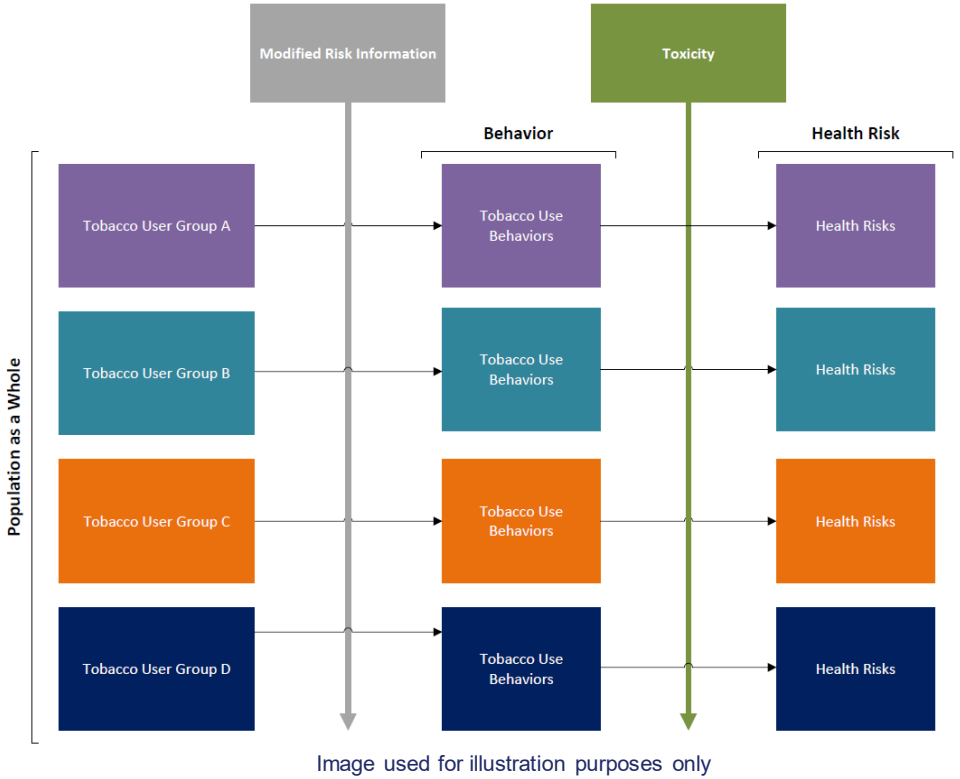


Image used for illustration purposes only

ADDITIONAL CONSIDERATIONS

- An MRTP order is for a specific product, not for a class of products
- Evaluations are in the context of a specific product and specific modified risk claim
- Form and wording of the claim have a critical impact on the final decision

REVIEW OF MODIFIED RISK INFORMATION

- FDA evaluates all information and statements on the proposed label, labeling, and advertising as part of its scientific review.
- This review includes, but is not limited to, an evaluation of the applicant's label, labeling, and advertising for modified risk claims even if those claims were not specifically identified by the applicant in its request for authorization.

SAMPLES OF MODIFIED RISK CLAIMS IN MRTPAs

"Smokers who **switch completely** from cigarettes to Camel SNUS can significantly reduce their risk of lung cancer, oral cancer, respiratory disease, and heart disease."

"Using General Snus instead of cigarettes puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis."

"Scientific studies have shown that Camel SNUS contains less of the harmful chemicals than cigarette smoke."

"Scientific studies have shown that switching completely from cigarettes to the IQOS system significantly reduces your body's exposure to harmful or potentially harmful chemicals."

"NO SMOKE = LESS RISK"

"Scientific studies have shown that Camel SNUS contains fewer carcinogens than cigarette smoke."

"IF YOU SMOKE, CONSIDER THIS: Switching completely to this product from cigarettes reduces risk of lung cancer."

POSTMARKET SURVEILLANCE AND STUDIES (PMSS)

- Each applicant who receives a risk modification or exposure modification order must conduct postmarket surveillance and studies (Section 911(g)(2)(C)(ii) and (i)(1))
- Allows for the evaluation of the effect of issuance of an order on consumer perception, behavior, and health, and enables FDA to review the accuracy of determinations upon which the order was based
  - Data on real-world use of the MRTP
  - Tobacco-related adverse events
  - Longer-term assessment of exposure and health outcomes
  - Ongoing assessment of tobacco use behavior
- Applicants are encouraged to submit with MRTPAs draft protocols and/or detailed outlines of PMSS so a final version of the protocols can be approved in a timely manner if an order is granted
- Applicants must submit results of PMSS annually

LESSONS LEARNED

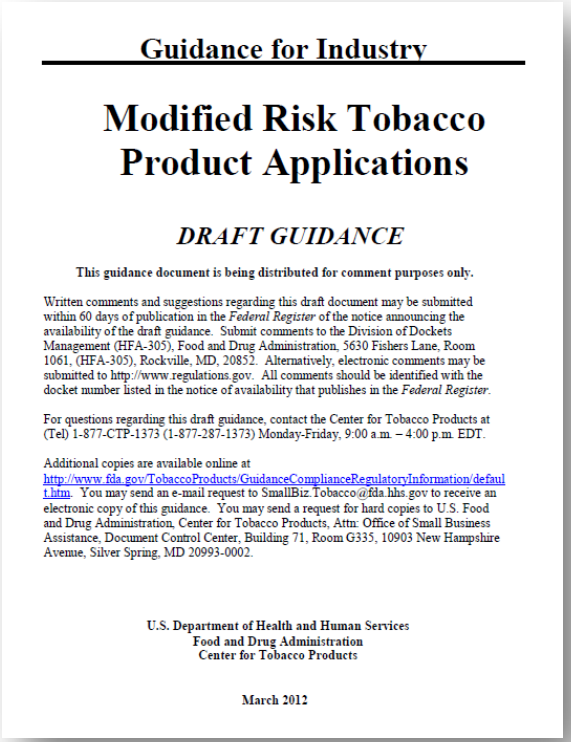
As we gain more experience with review of MRTPAs, we are looking for ways to improve efficiency in the submission and review of applications. Examples of efforts to improve efficiency include:

- Clarification of FDA's interpretation of the submission of "all documents" as required under 911(d)(5)
- Maximizing the efficiency and productivity of TPSAC meetings by…
  - Focusing the scope of the meeting to select scientific issues from the applications
  - Producing focused FDA background materials for the committee
  - Streamlining FDA presentations
  - Crafting clear, focused questions for the committee
  - Bringing in additional subject matter expertise as needed

COMMUNICATING LESSONS LEARNED

We are clarifying our expectations and communicating opportunities for improvement to industry in various ways, including…

- Public meetings (e.g., Tobacco Product Application Review Meeting, October 2018)
- Draft guidance (Modified Risk Tobacco Product Applications, 2012)



Guidance for Industry

Modified Risk Tobacco Product Applications

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Written comments and suggestions regarding this draft document may be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to http://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft guidance, contact the Center for Tobacco Products at (Tel) 1-877-CTP-1373 (1-877-287-1373) Monday-Friday, 9:00 a.m. – 4:00 p.m. EDT.

Additional copies are available online at http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/default.htm. You may send an e-mail request to SmallBiz.Tobacco@fda.hhs.gov to receive an electronic copy of this guidance. You may send a request for hard copies to U.S. Food and Drug Administration, Center for Tobacco Products, Attn: Office of Small Business Assistance, Document Control Center, Building 71, Room G335, 10903 New Hampshire Avenue, Silver Spring, MD 20993-0002.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products

March 2012

THE END