



MODIFIED RISK TOBACCO PRODUCT MARKETING DECISIONS

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- Statutory framework for Modified Risk Tobacco Products (MRTP)
- How was this framework applied to the Swedish Match North America (SMNA) MRTPAs
- SMNA MRTPA decisions
- TPSAC process and lessons learned



STATUTORY FRAMEWORK FOR MODIFIED RISK TOBACCO PRODUCTS

MODIFIED RISK TOBACCO PRODUCTS (MRTPS) DEFINED



- Tobacco products sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products
 - Label, labeling or advertising represents that:
 - The product is less harmful or presents a lower risk of tobacco-related disease
 - The product or its smoke contains a reduced level of, presents a reduced exposure to, or does not contain/is free of a substance

THE STANDARD FOR MODIFIED RISK

The FD&C Act requires FDA to determine if a proposed MRTP, as it is actually used by consumers, will:

- (1) significantly reduce harm and the risk of tobacco-related disease to individuals and
- (2) benefit the health of the population as a whole



SPECIAL RULE FOR CERTAIN PRODUCTS



- The FD&C Act allows FDA to issue an order if :
 - 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 without conducting long-term epidemiological studies; and
 - scientific evidence that is available demonstrates that a reduction in morbidity or mortality is reasonably likely.

THE FOUR-STEP 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. Will the MRTP significantly reduce the harm and risk of tobacco-related disease to individual tobacco users?
3. How do consumer's perception, understanding, and comprehension of the modified risk information impact potential benefits and harms?
4. What are the potential benefits and harms to the health of the population as a whole?

MRTP CONTEXT

- 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.





HOW WAS THIS FRAMEWORK APPLIED TO THE SWEDISH MATCH MRTPA?

OVERVIEW OF SWEDISH MATCH NORTH AMERICA (SMNA) APPLICATIONS



- Modified Risk Tobacco Product (MRTP) applications were received by FDA on June 10th 2014 for the following tobacco products:
 - General Loose
 - General Dry Mint Portion Original Mini
 - General Portion Original Large
 - General Classic Blend Portion White Large – 15 ct*
 - General Classic Blend Portion White Large – 12 ct
 - General Mint Portion White Large
 - General Nordic Mint Portion White Large – 15 ct*
 - General Nordic Mint Portion White Large – 12 ct
 - General Portion White Large
 - General Wintergreen Portion White Large

** Subsequently withdrawn by the applicant.*

SMNA MRTPA INFORMATION



- The SMNA MRTPAs contained information from various types of scientific studies:
 - Product analyses (chemistry, engineering, microbiology)
 - Toxicological assessments
 - Pharmacokinetic studies
 - Clinical trials (for impact on cessation)
 - Epidemiological studies (health and behavior)
 - Consumer perception and comprehension studies
 - Statistical modeling
 - Plans for postmarket surveillance and studies



SMNA MRTPA REQUEST

- **Warnings to be removed:**

- *WARNING: This product can cause gum disease and tooth loss*
- *WARNING: This product can cause mouth cancer*



- **Revision to the warning:**

- *From: WARNING: This product is a not a safe alternative to cigarettes*
- *To: WARNING: No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes*

- **SMNA did not request to change the required warning:**

- *WARNING: Smokeless tobacco is addictive*

SMNA MRTPA BASIS OF PROPOSAL



- Similar products and users in Norway and Sweden:
 - Conform to the same standards
 - Pose the same level of exposures of harmful constituents to users
 - Users of these products will experience the same health outcomes
- Have relatively low levels of harmful constituents, particularly TSNAs
- In Sweden, smoking rates among men and rates of tobacco-related disease and death are lower
- Lower smoking rates are due to a “grassroots” movement among Swedes

FDA EVALUATION OF THE SMNA MRTPAS



- FDA completed the following activities during the application review process:
 - Reviewed applications as an interdisciplinary team with expertise in chemistry, engineering, microbiology, toxicology, environmental science, pharmacology, medicine, epidemiology, social science, and statistics.
 - Requested clarification on specific topics/questions from the applicant.
 - Reviewed public comments received on redacted applications.
 - Convened the TPSAC and integrated findings from the committee.
 - Evaluated all relevant evidence to determine whether the statutory requirements were met.

FDA FINDING ON GUM DISEASE AND TOOTH LOSS



- The warning “*WARNING: This product can cause gum disease and tooth loss*” is currently required for all smokeless tobacco products.
 - Smokeless tobacco products have been required to bear a warning related to gum disease and tooth loss since 1986.
- Omission of this warning represents an implied modified risk claim that the eight General Snus products, unlike other smokeless tobacco products, cannot cause gum disease or tooth loss.
- Epidemiological evidence indicates that use of these products increases the risks of certain outcomes classified as gum disease or tooth loss, or precursors to gum disease and tooth loss.

FDA FINDING ON GUM DISEASE AND TOOTH LOSS



- There is little biologically plausible reason to expect that outcomes related to gum and teeth of users would differ between these products and other smokeless tobacco products.
- The evidence supports the statement that smokeless tobacco products in general and these products in particular can cause gum disease and tooth loss.
- The evidence does not substantiate the proposed implied modified risk claim.

FDA FINDING ON MOUTH CANCER



- The warning “*WARNING: This product can cause mouth cancer*” is currently required for all smokeless tobacco products.
 - Smokeless tobacco products have been required to bear a warning related to mouth cancer since 1986.
- Omission of this warning represents an implied modified risk claim that the eight General Snus products, unlike other smokeless tobacco products, cannot cause mouth cancer.
- Although epidemiological studies observed a lack of a consistent association, the most recently published study presented in the applications reported a large and statistically significant association.
 - Inconsistency across studies may be due to the lack of precision in the estimates of risk, the variability in the definition of oral cancer, and other study limitations.

FDA FINDING ON MOUTH CANCER



- The products contain significantly lower levels of carcinogens than other smokeless tobacco products on the market; however, they still expose users to elevated levels of harmful carcinogens.
- NNN, in particular, is a potent oral carcinogen and no biologically plausible rationale was provided for why these products do not pose an increased risk of oral cancer.
- Available scientific evidence supports the statement that smokeless tobacco products in general and these products in particular can cause mouth cancer.
- The evidence does not substantiate the proposed implied modified risk claim.

FDA FINDING ON RISK RELATIVE TO CIGARETTES



- The eight General Snus products can expose users to levels of constituents at levels lower than smoking.
- Evidence supports that exclusive use of the eight General Snus products as compared to smoking cigarettes may significantly reduce harm and the risk of certain tobacco-related disease to individual tobacco users.
 - There are clear, substantial differences in the risk of certain diseases, such as lung cancer and respiratory disease.
 - The reduction in health risks to an individual is dependent on patterns of use of the snus products, i.e., whether individual users switch completely to the use of the eight General Snus products.
- The evidence partially substantiates the proposed modified risk claim.

ADDITIONAL SELECT FDA FINDINGS – IMPACTS ON BEHAVIOR



- The information on the behavior of the Swedish and Norwegian populations with respect to snus type products has limited applicability to the U.S. population.
 - Snus products are currently available in the U.S., with limited uptake.
 - Snus holds cultural and traditional significance among Swedish users.
 - SMNA describes a historical shift away from smoking to snus use that occurred in Sweden, but does not provide evidence or information to suggest that a similar process could or would occur in the U.S.
 - Labeling and marketing of snus in Sweden has not referred to the product as reduced risk.

ADDITIONAL SELECT FDA FINDINGS – CONSUMER PERCEPTION STUDY



- The Consumer Perception Study conducted by SMNA does not provide sufficient insight as to what consumers understand about the risks of using the eight General Snus products after viewing the modified risk information, especially in the context of a warning.
 - The applicant did not provide evidence regarding how the removal of warnings would impact consumer behavior or comprehension.
 - For the revised warning statement, the applicant did not assess the impact of the context – within a warning or as a stand-alone promotional statement, or in the context of an advertisement – of the modified risk information.
 - The stimuli (images of the product package with the label) included in the study did not present the actual proposed revised warning statement verbatim.

ADDITIONAL SELECT FDA FINDINGS – POPULATION MODEL



- Although the applicant modeled a number of different scenarios of the impact to users and non-users, some resulted in population health benefits and some resulted in population health harms, and the applicant provided inadequate evidence as to which scenarios were more or less likely.



SMNA MRTTP DECISIONS



SMNA MRTP DECISION



- With respect to the request to remove the gum disease and tooth loss warning, FDA concluded that SMNA did not demonstrate that, as actually used by consumers, the product would significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole.

This request was denied.

SMNA MRTPA DECISION



- With respect to the requests to remove the mouth cancer warning and revise the “not a safe alternative” warning, in their present form, the applications do not contain sufficient evidence to satisfy the modified risk standard.
- However, the applications could be amended in several ways
 - changing the proposed claims
 - supplementing the evidence, and
 - conducting new studies

which could provide sufficient evidence to support issuance of modified risk orders relating to mouth cancer and health risks compared to cigarettes for these tobacco products.

MODIFIED RISK TOBACCO PRODUCT MARKETING DECISIONS



- While the FDA isn't authorizing these specific products as MRTPs at this time, the lessons learned through these first applications provide key insights for a potential path forward through an amended application and for others considering submitting an application.
- The FDA is committed to authorizing modified risk tobacco products for any company which submits adequate data demonstrating that the standard has been met.

TPSAC PROCESS AND LESSONS LEARNED

TPSAC MEETING ON SMNA MRTP APPLICATIONS



- Pursuant to Section 911(f) of the FD&C Act, FDA referred the MRTPAs to the TPSAC, and the TPSAC discussed the applications during an open public committee meeting held on April 9-10, 2015.
- At the meeting, the Committee discussed the MRTPAs, including the adequacy of the scientific evidence to support the proposed modified risk marketing.

SCOPE OF MRTPA TPSAC MEETINGS



- FDA reviews encompass the entirety of the materials included in the MRTPAs.
- Although the entire applications are referred to the Committee, FDA presentations to the Committee may not include all issues relevant to the final regulatory recommendation and instead are intended to focus on issues identified by the Agency for discussion by the Committee.
- Based on its review, FDA will identify critical scientific issues to bring to TPSAC for discussion, directly related to the factors FDA must consider when taking an action.

TOPICS FOR DISCUSSION AT APRIL 2015 TPSAC MEETING



- With respect to the relative health risks to individuals, FDA brought to TPSAC questions related to:
 - The strength of association between snus use and the risk of tooth loss and gum disease
 - The strength of association between snus use and the risk of oral cancers.
 - The risks of snus use as compared to cigarettes.
- With respect to the impacts on initiation and cessation, FDA brought to TPSAC questions related to:
 - The applicability of the Swedish experience to infer impacts on the U.S. population.

TOPICS FOR DISCUSSION AT APRIL 2015 TPSAC MEETING



- With respect to the ability of the public to comprehend the modified risk information, FDA brought to TPSAC questions related to:
 - The impacts of providing modified risk information in the context of a warning.
- FDA also sought recommendations from TPSAC on postmarket surveillance and studies, should FDA issue an order permitting the marketing of the products as modified risk.

PRIOR TO THE TPSAC MEETING



- Committee was provided with full unredacted application (>100,000 pages)
- Committee received FDA background materials, including:
 - 65-page briefing document, describing FDA's preliminary review findings and draft topics for discussion
 - Modified Risk Tobacco Product Applications Draft Guidance for Industry
 - Section 911 of the Federal Food Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act
- Written submissions to the Committee from the public.
- Committee received 78-page Swedish Match advisory committee briefing document.

MEETING PARTICIPANTS



TPSAC Members and Temporary Members

- Voting TPSAC members
- Industry representatives
- Ex-Officio members
- Subject matter experts
 - Paolo Boffetta, MD, MPH – Physician and epidemiologist with expertise in smokeless tobacco use and cancer risk.
 - Scott Tomar, DMD, MPH, DrPH – Dentist and expert on the behavioral patterns and health risks of smokeless tobacco products.

Presenters

- FDA officials and reviewers
- Representatives for the applicant

PRESENTATIONS BY SMNA



- Introduction and Overview
- Scientific Literature Review Conducted by ENVIRON and Characterizing the Swedish Human Health Evidence
- Description of the Evidence: Clinical Trials, Premarket Consumer Perception Study, and the Dynamic Population Modeler
- GOTHIA TEK® Standards

PRESENTATIONS BY FDA



- Statutory Framework for MRTPAs and Summary of the Scientific Review Process
- Epidemiological Evidence Related to the SMNA MRTPA Snus Products and Gum Disease or Tooth Loss
- Epidemiological Evidence Related to SMNA Snus and Mouth Cancer
- Overall Health Effects of Swedish Match Snus Products
- Applicability of Swedish Epidemiological Data to the United States
- Consumer Understanding and Implications of Modified Risk Information in a Warning Label
- Postmarket Surveillance and Studies

- FDA made the MRTPAs available for public comment and summarized scientific comments received through the docket at the TPSAC meeting.
- FDA solicited written comments in response to the TPSAC meeting announcement, which were provided to the Committee in advance of the meeting.
- Day 2 of the TPSAC meeting provided an additional opportunity for oral public comment to the Committee.

HOW FDA UTILIZES THIS INFORMATION



- TPSAC deliberation and voting are weighed in FDA's evaluation of the evidence.
- TPSAC votes are non-binding, but inform FDA's assessment and determination.
- Findings from the committee are cited in the Technical Project Lead review summarizing FDA's decision.

CLARIFYING QUESTIONS?

