22ND CENTURY GROUP INC. MODIFIED RISK TOBACCO PRODUCT APPLICATIONS (MRTPAS)

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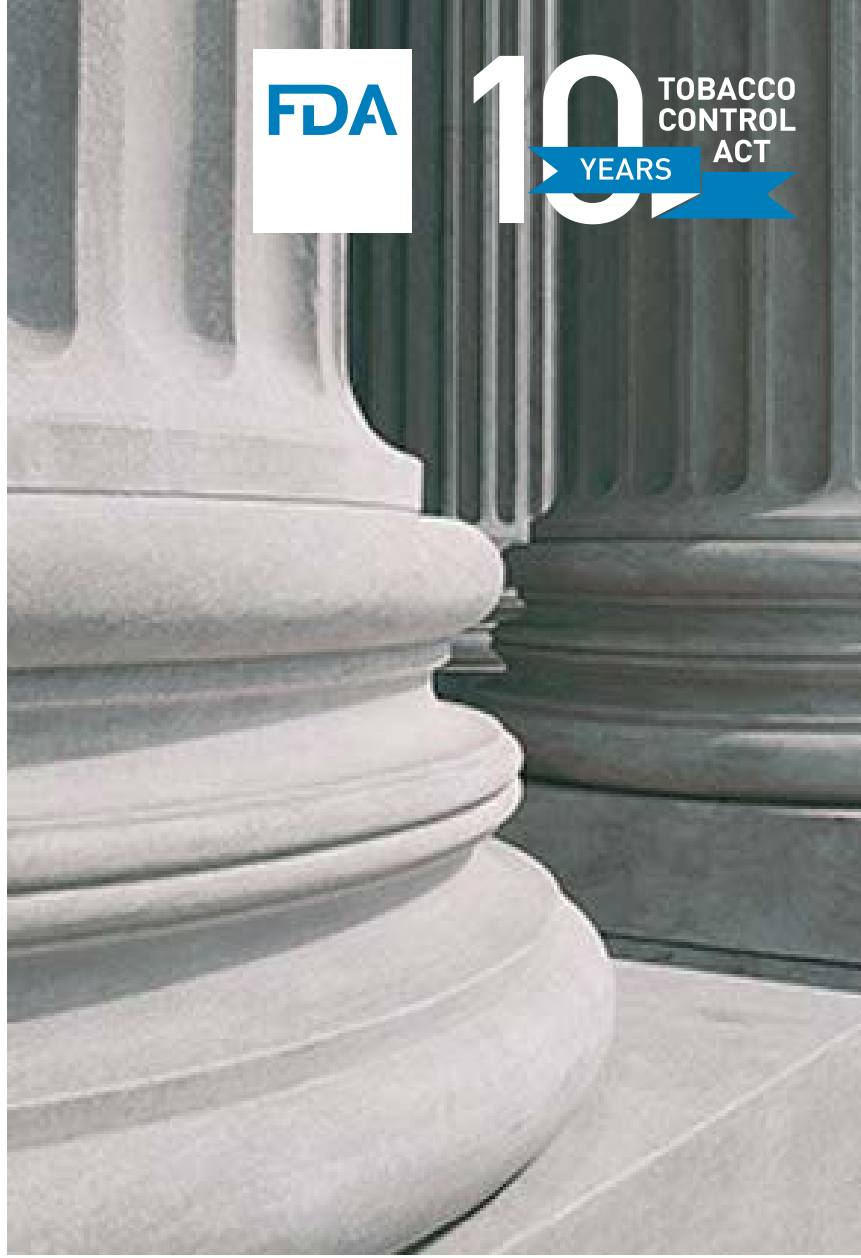

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- This may contain assessments and/or conclusions and recommendations written by individual FDA reviewers.
- Such conclusions and recommendations do not necessarily represent the final position of the individual reviewers, nor do they necessarily represent the final position of the Review Division or Office.
- We are referring 22nd Century Group Inc.'s MRTPAs for VLN™ King and VLN™ Menthol King cigarettes to TPSAC in order to gain the Committee's insights and recommendations.
- This presentation may not include all issues relevant to FDA's decision on the applications and instead is intended to focus on issues identified by FDA for discussion by the TPSAC.
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AGENDA

MRTP Application Overview

Section 910(b) FD&C Act

Background & summary of PMTA application evaluation

Section 911 FD&C Act

Summary of select requirements from Section 911 of the FD&C Act

TPSAC Discussion questions

22ND CENTURY GROUP INC. MRTP APPLICATIONS

- 22nd Century Group, Inc. submitted MRTPAs to market two very low nicotine (VLN) cigarettes: VLN™ King and VLN™ Menthol King, with reduced exposure claims.

MODIFIED RISK CLAIMS IDENTIFIED BY APPLICANT

1	95% less nicotine
2	Helps reduce your nicotine consumption
3	…greatly reduces your nicotine consumption
"Voluntary Disclaimer"	Nicotine is addictive. Less nicotine does NOT mean safer. All cigarettes can cause disease and death

22ND CENTURY GROUP INC. PRODUCT APPLICATIONS: PMTA

Section 910(b) FD&C Act

On December 17, 2019, FDA granted PMTA orders for the applicant to market these same products without modified risk information.

- FDA found that at this time, permitting the marketing of the products is appropriate for the protection of the public health.
  - In the PMTAs, the applicant uses the brand “Moonlight™.”
  - In the MRTPAs, the applicant uses the brand “VLN™.”
  - Both the PMTAs and the MRTPAs refer to research on SPECTRUM and Quest Very Low Nicotine Content (VLNC) cigarettes, which are similar to their products.

HIGHLIGHTS FROM PMTA REVIEW

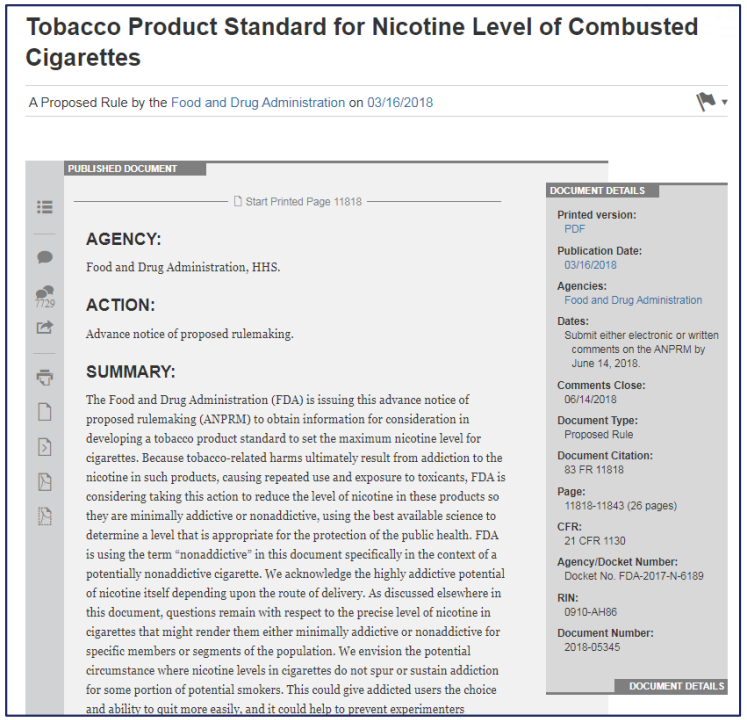
- Overall toxicant-associated noncancer hazards and cancer risks due to use of VLN™ cigarettes are likely similar to the comparison normal nicotine content cigarettes *if they are used in the same way.*
  - **It is likely that smokers who primarily use VLN™ will smoke less.**
- VLN™ cigarettes have a lower abuse liability than normal nicotine content cigarettes.
- Use of VLNC cigarettes is not associated with compensatory smoking in general or vulnerable populations.
- Smokers may not switch completely to VLN™ cigarettes because of low subjective appeal, increased craving, and withdrawal.

HIGHLIGHTS FROM PMTA REVIEW

- Exclusive and dual product users who primarily use VLNC cigarettes would likely:
  - Reduce their exposure to nicotine.
  - Reduce their cigarettes per day.
  - Reduce their nicotine dependence.
- Switching to VLNC cigarettes may facilitate abstinence in smokers by increasing motivation to quit and quit attempts.
  - Concurrent use of nicotine replacement therapy (NRT) and behavioral intervention may improve these outcomes.
- Findings apply to smokers who use menthol and non-menthol VLN™ cigarettes.

FDA'S ADVANCED NOTICE OF PROPOSED RULEMAKING FOR SETTING MAXIMUM NICOTINE LEVELS IN CIGARETTES

- FDA issued an advanced noticed of proposed rulemaking (ANPRM) for setting a maximum nicotine level in cigarettes on March 16, 2019.
  - FDA issued this ANPRM to obtain information for consideration.
- FDA does not have information on next steps at this time.
- We ask TPSAC members to assume that such a rule has <u>not</u> gone into effect when discussing these MRTPAs.



Tobacco Product Standard for Nicotine Level of Combusted Cigarettes

A Proposed Rule by the Food and Drug Administration on 03/16/2018

PUBLISHED DOCUMENT

Start Printed Page 11818

AGENCY:

Food and Drug Administration, HHS.

ACTION:

Advance notice of proposed rulemaking.

SUMMARY:

The Food and Drug Administration (FDA) is issuing this advance notice of proposed rulemaking (ANPRM) to obtain information for consideration in developing a tobacco product standard to set the maximum nicotine level for cigarettes. Because tobacco-related harms ultimately result from addiction to the nicotine in such products, causing repeated use and exposure to toxicants, FDA is considering taking this action to reduce the level of nicotine in these products so they are minimally addictive or nonaddictive, using the best available science to determine a level that is appropriate for the protection of the public health. FDA is using the term "nonaddictive" in this document specifically in the context of a potentially nonaddictive cigarette. We acknowledge the highly addictive potential of nicotine itself depending upon the route of delivery. As discussed elsewhere in this document, questions remain with respect to the precise level of nicotine in cigarettes that might render them either minimally addictive or nonaddictive for specific members or segments of the population. We envision the potential circumstance where nicotine levels in cigarettes do not spur or sustain addiction for some portion of potential smokers. This could give addicted users the choice and ability to quit more easily, and it could help to prevent experimenters

DOCUMENT DETAILS

Printed version: PDF

Publication Date: 03/16/2018

Agencies: Food and Drug Administration

Dates: Submit either electronic or written comments on the ANPRM by June 14, 2018.

Comments Close: 06/14/2018

Document Type: Proposed Rule

Document Citation: 83 FR 11818

Page: 11818-11843 (26 pages)

CFR: 21 CFR 1130

Agency/Docket Number: Docket No. FDA-2017-N-6189

RIN: 0910-AH86

Document Number: 2018-05345

DOCUMENT DETAILS

SELECT REQUIREMENTS FROM SECTION 911 OF THE FD&C ACT

(g)(2)(A)(iv)

MORBIDITY & MORTALITY

The scientific evidence that is available without conducting long-term epidemiological studies demonstrates that **a measurable and substantial reduction in morbidity or mortality** among individual tobacco users is reasonably likely in subsequent studies.

(g)(2)(B)(iv)

EFFECT ON POPULATION

Issuance of an order with respect to the application is expected to **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.

SELECT REQUIREMENTS FROM SECTION 911 OF THE FD&C ACT

(g)(2)(B)(iii)

UNDERSTANDING

Testing of actual consumer perception shows that, as the applicant proposes to label and market the product, **consumers will not be misled** into believing that the product:

- is or has been demonstrated to be less harmful; or
- presents or has been demonstrated to present less of a risk of disease than 1 or more other commercially marketed tobacco products.

(h)(1)

UNDERSTANDING

The advertising/labeling **enables the public** to:

- comprehend the information concerning modified risk, and
- understand the relative significance of such information
  - in the context of total health, and
  - in relation to all tobacco-related diseases and health conditions.

OTHER REQUIREMENTS FROM SECTION 911 OF THE FD&C ACT

Other requirements that we will not be specifically focusing on today include 911(g)(2)(B)(i)&(ii):

(i) The magnitude of **overall reductions in exposure to the substance(s) is substantial**, such substance or substances are harmful, and the product, as actually used, exposes consumers to the specified reduced level of the substance(s)

(ii) The product, as actually used by consumers, **will not expose them to higher levels of other harmful substances** compared to similar types of tobacco products on the market, unless such increases are minimal and the reasonably likely overall impact of product use remains a substantial and measurable reduction in overall morbidity and mortality among individual tobacco users

TPSAC DISCUSSION QUESTIONS

DISCUSSION QUESTIONS

1 MORBIDITY & MORTALITY

Discuss the likelihood that reductions in dependence translate into substantial reductions in morbidities and mortality among individual tobacco users.

2 EFFECT ON NONSMOKERS

Discuss the extent to which the following groups are likely to try and progress to regularly using the proposed modified risk tobacco products:

- Never smokers
- Former smokers

3 EFFECT ON SMOKERS

Discuss the extent to which the following groups will dual use the proposed modified risk products with their usual brand of cigarettes or exclusively use the proposed modified risk products:

- Cigarette smokers who want to quit smoking
- Cigarette smokers who do not want to quit smoking

4 UNDERSTANDING

Discuss whether the labeling enables consumers to accurately understand the following effects of using the products:

- Addiction risk
- Disease risks

Q&A ABOUT GRANTING MRTPA ORDERS

Has FDA restricted how these products are marketed?

- Yes, FDA already imposed certain marketing restrictions for these products in the PMTA orders (e.g., to help ensure advertising is targeted only to adults).

How long would an order last?

- Under Section 911(g)(2), the maximum duration of an order is 5 years.
- There is no minimum length of time for an order.

Can FDA require certain things to be studied in postmarket surveillance?

- Yes, FDA can require specific studies.
- FDA required specific reports related to advertising under the PMTA orders granted for these products.

THE END