Tobacco Products Scientific Advisory Committee (TPSAC)

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Tobacco Products (CTP)
FDA White Oak Conference Center
Building 31, Room 1503
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

February 14, 2020

These summary minutes for the February 14, 2020 meeting of the Tobacco Products Scientific Advisory Committee of the Food and Drug Administration were approved on March 24, 2020.

I certify that I attended the February 14, 2020 meeting of the Tobacco Products Scientific Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

_____/s/_____

Serina A. Hunter-Thomas, MSA, RN
Designated Federal Officer, TPSAC

_____/s/_____

Robin J. Mermelstein, PhD
Chair, TPSAC

Meeting of the Tobacco Products Scientific Advisory Committee

February 14, 2020

The Tobacco Products Scientific Advisory Committee (TPSAC) of the Food and Drug Administration, Center for Tobacco Products (CTP) met on February 14, 2020 at the FDA White Oak Conference Center, Building 31, Room 1503, 10903 New Hampshire Avenue, Silver Spring, MD 20993-0002. Prior to the meeting, committee members and invited participants were provided copies of the background materials from the FDA and the applicant, and the submissions from the public. The meeting was called to order by Robin J. Mermelstein, PhD (Chair); the conflict of interest statement was read into the record by Serina Hunter-Thomas, MSA, RN (Designated Federal Officer). There were approximately 50 persons in attendance. There were three speakers for the Open Public Hearing session.

Agenda: *On February 14,2020 the Committee discussed modified risk tobacco product applications (MRTPAs) submitted by 22nd Century Group Inc. for the following cigarette tobacco products; MR0000159: VLN™ King, and MR0000160: VLN™ Menthol King*

Attendance:

TPSAC Members Present (Voting):
Robin J. Mermelstein, PhD (Chair)
Laura J. Bierut, MD
Sonia A. Duffy, PhD, RN, FAAN (*Representative of the General Public)*
Sara P. Herndon, MPH (*Employee of a state or local government or of the Federal Government*)
Deborah J. Ossip, PhD (via phone)
James F. Thrasher, PhD
Kenneth E. Warner, PhD
Michael Weitzman, MD

Industry Representative Members Present (Non-voting):
William Andy Bailey, PhD *(Representative of the interests of tobacco growers)*
Sarah E. Evans, PhD, MS *(Representative of the interests of small business tobacco manufacturing industry)*
Michael Ogden, PhD (*Representative of the interests of the tobacco manufacturing industry)*

Ex Officio Participants Present (Non-Voting):
Alberta Becenti, MPH (IHS)
Brian King, PhD, MPH (CDC)
Kay L. Wanke, PhD, MPH (NIH)

Consultants Present (Non-Voting):
Eric Donny, PhD
Dorothy Hatsukami, PhD

Speaker:
Justin Byron, PhD

FDA Participants/Speakers (Non-Voting):
Mitchell Zeller, JD
Benjamin Apelberg, PhD
Cindy Tworek, PhD, MPH
Mollie Miller, PhD
Alexander Persoskie, PhD

Designated Federal Officer:
Serina A. Hunter-Thomas, MSA, RN

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The agenda on February 14, 2020 was as follows:

February 14, 2020

Call to Order/Opening Remarks and Introduction of Committee	Robin J. Mermelstein, PhD Chair, TPSAC
Administrative Announcements and Conflict of Interest Statement	Serina Hunter-Thomas, MSA, RN Designated Federal Officer Office of Science, FDA/CTP
FDA Presentation: 22nd Century Group Inc. Modified Risk Tobacco Product Applications (MRTPAs)	Cindy Tworek, PhD, MPH Technical Project Lead, 22nd Century Group Inc. Branch Chief, Division of Population Health Science Office of Science, FDA/CTP
22nd Century Group Inc. Presentations: • Introduction • Product and Claims Overview • Pre-market Tobacco Product Application • Modified Exposure Statutory Requirements Under 911(g)(2)	John D. Pritchard, BSc (Hons), MSc, CBiol, MRSB Vice President of Regulatory Science 22nd Century Group, Inc.
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22nd Century Group Inc. Presentations Cont'd:	Ed Carmines, PhD Carmines Consulting, LLC
• Reductions in Morbidity and Mortality • Consumer Perceptions • Consumer Perception Studies • Consumer Interest and Intention to Use: - Never Smokers and Former Smokers	
• Conclusions	John D. Pritchard, BSc (Hons), MSc, CBiol, MRSB Vice President of Regulatory Science 22nd Century Group, Inc.
Break	
Open Public Hearing	
FDA Presentation: Evaluating VLN™ Cigarettes as MRTPs: Considerations of Morbidity, Mortality and Population Health	Mollie Miller, PhD Pharmacologist Division of Individual Health Science Office of Science, FDA/CTP
Discussion of Questions # 1 and 2	TPSAC
Lunch	
Discussion of Question # 3	TPSAC
FDA Presentations: Investigating and Addressing the Perceived Risk of Nicotine and Very Low Nicotine Content Cigarettes	Justin Byron, PhD Assistant Professor, Family Medicine School of Medicine Adjunct Assistant Professor, Health Behavior Gillings School of Global Public Health University of North Carolina at Chapel Hill
Consumer Understanding of the Modified Risk Information	Alexander Persoskie, PhD Social Scientist Division of Population Health Science Office of Science, FDA/CTP
Discussion of Question # 4	TPSAC
Adjourn	

Open Public Hearing Session Speakers:

- Nina Zeldes, PhD, National Center for Health Research
- Michael F. Borgerding, PhD, RAI Services Company
- Matthew L. Myers, Campaign for Tobacco-Free Kids

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***Questions to the Committee*:**

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

   TPSAC discussed questions about biomarkers and topographical data and if there were enough data available to substantially conclude that a reduction in dependence would then translate into a reduction in morbidity and mortality.

   One member said they thought that a reduction in smoking was likely to translate to a reduction in morbidity and mortality.
   Another member stated that there are actually two pathways to reduced morbidity and mortality. One is the reduction in cigarettes per day, and the other pathway is the reduction in dependence, which can lead to an increase in cessation. Another member noted that while there was a dose-response relationship for cancer, there was not for cardiovascular disease. Another agreed that not all morbidities were reduced.

   The committee noted that the clinical studies on very low nicotine content cigarettes instructed participants to switch completely to VLNC cigarettes. Without instructions for VLN cigarette use, results obtained in these clinical studies are likely not representative of a situation in which individuals do not receive instructions for use. The committee recommended that information be added to VLN cigarettes to clarify that smokers should switch completely to the products in order to achieve results similar to those obtained in the clinical literature.

   In summary for this question, TPSAC discussed that there seemed to be some compelling information to make the inference that as dependence gets reduced from very low nicotine content cigarettes, other things follow, which may lead to some reductions in morbidities and likely lead to reduction in mortality at the individual level.

   The committee also discussed the dual use issue and alternatives to quitting tobacco use.

2. Discuss the extent to which the following groups are likely to try and progress to regularly using the proposed modified risk tobacco products:
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- Never smokers
- Former smokers

The committee expressed concerns about there being no evidence with testing or clinical data about use among young people. TPSAC stated that they would like some kind of strategy developed to collect data from youth regarding these kinds of modified risk products, noting that there is a need for adolescent data, but that there are ethical issues with conducting this research.

The committee discussed the difference between trial and experimentation and progression to use. Although there are no direct data about the product in adolescents, there are data from adolescent models and other users to suggest that the lower nicotine products do not result in higher abuse liability, and the committee felt that it seems unlikely that there would be progression beyond initial trial to regular use of this product among never smokers. One committee member also stated that they thought former smokers would not be interested in the product, and did not have concerns about them.

TPSAC expressed concerns regarding the advertising and imagery being appealing to youth. There was discussion regarding the brand name of Moonlight and the committee mentioned that the word "light" has come up before in previous meetings. FDA staff clarified that the application review is under VLN as the name, not Moonlight.

Some committee members suggested that the wording of Question 2 include adding "or conventional cigarettes" at the end. FDA clarified that the questions cannot be changed at this time, but that committee members can discuss this issue for the record. TPSAC noted that there is a lack of data needed to draw conclusions on the likelihood of progression to either continued VLN or conventional cigarette use after experimentation with VLN cigarettes.

3. 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

Members discussed how compliance might differ among smokers who do want to quit, noting that the members' clinical studies on the topic did not look at this.

TPSAC discussed that the probability of dual use is likely high in scenarios where both usual brand cigarettes and low nicotine content cigarettes are available. Dual use may occur for both smokers who want to quit and smokers who don't want to quit, and the extent of dual use may vary. TPSAC discussed that cigarette smokers

who do not want to quit smoking may dual use VLN and usual brand cigarettes believing that it may reduce their nicotine exposure and lower their health risks. They discussed that for smokers who do want to quit, they may use the product on the road to quitting.

TPSAC discussed that instruction of completely switching is missing, and if this information/instruction was provided, or clearer, it could potentially decrease dual use and cigarette-related diseases.

4. Discuss whether the labeling enables consumers to accurately understand the following effects of using the products:
   - Addiction risk
   - Disease risks

Regarding addiction risk, TPSAC generally agreed that the labeling would enable consumers to understand the addiction risk from smoking VLN cigarettes. However, one member pointed out that addiction risk is different for everyone; that is, it's not all equal. There are data to support this in genetic studies. Therefore, the response to nicotine and perceptions of risk will differ from individual to individual.

Regarding disease risks, TPSAC discussed the applicant's study results showing that U.S. adults rated VLN cigarettes as lower in disease risks compared to other cigarettes. FDA presented two alternative interpretations of these findings to TPSAC and asked for committee members' perspectives on whether one of these interpretations was more likely to be correct than the other: (1) participants *incorrectly* rated VLN cigarettes as lower in disease risks than other cigarettes because participants believed the lower nicotine content would allow people to smoke VLN cigarettes in the same way as other cigarettes without incurring the same disease risks, or (2) participants *correctly* rated VLN cigarettes as lower in disease risks than other cigarettes because participants understood that, because of VLN's lower addiction risk, people would smoke fewer VLN cigarettes or would smoke VLN for a shorter duration than other cigarettes, causing fewer diseases. TPSAC members stated that the first interpretation is more likely to be correct, because it is unlikely that participants thought through the products' addictiveness (and the corresponding effects on use frequency and duration) when rating the disease risks of smoking VLN cigarettes. TPSAC members suggested that participants' lower ratings of disease risk from VLN cigarettes could be attributed to widespread misperceptions of nicotine, and that the proposed VLN labeling would not enable consumers to understand the products' disease risks.

Three members noted issues with the "voluntary warning" and needing more research on it. One member said more research is needed on what might reduce misperception of disease risk, because the "voluntary warning" is not sufficient. Another said that the "voluntary warning" was problematic because it looks like a legal disclaimer and there was no evidence of its impact. Another said there was a

need to test ways to communicate that the product is equally risky, such as several reasonable strategies tested with the most promising one selected.

The committee had consensus on the importance of providing accurate, specific information to the public about nicotine content, and that there are important benefits to educating the public about nicotine. The committee also noted, though, that misperceptions are common and that no one product is likely to overcome all the misperceptions about risk. Most members agreed that information about the product being low nicotine should not be withheld.

Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:

CTP/Tobacco Products Scientific Advisory
Day 1
https://collaboration.fda.gov/pwh9s8zp3kaf/
https://collaboration.fda.gov/popkv1ians57/
https://collaboration.fda.gov/pbhr25oh5ns1/