Technical Project Lead (TPL) Review:

SE0010524, SE0010525, SE0010526, SE0010532, and SE0010533

SE0010524: General Loose	
Package Type	Cardboard Can with Plastic Lid
Package Quantity	45 g
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	None
SE0010525: General Dry Mint Portion Original Mini	
Package Type	Plastic Can
Package Quantity	6 g
Portion Count	20 pouches
Portion Mass	300 mg
Portion Length	28 mm
Portion Width	14 mm
Portion Thickness	5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	Mint
SE0010526: General Portion Original Large	
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	33 mm
Portion Width	18 mm
Portion Thickness	6 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	None

[1] The applicant provided (b) (4) buckets to characterize the tobacco cut size. Therefore, the tobacco cut size cannot be represented with a single size value and corresponding range limit.

SE0010532: General Portion White Large	
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	34 mm
Portion Width	18 mm
Portion Thickness	5.5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	
SE0010533: General Wintergreen Portion White Large	
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	34 mm
Portion Width	18 mm
Portion Thickness	5.5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	Wintergreen
Common Attributes of SE Reports	
Applicant	Swedish Match North America, Inc.
Report Type	Regular
Product Category	Smokeless Tobacco
Product Sub-Category	Loose and portioned snus
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Digitally signed by Matthew R. Holman -S
Date: 2015.11.02 13:34:50 -05'00'

Matthew R. Holman, Ph.D.
Director
Division of Product Science

Signatory Decision:

☒ Concur with TPL recommendation and basis of recommendation

☐ Concur with TPL recommendation with additional comments (see separate memo)

☐ Do not concur with TPL recommendation (see separate memo)

Digitally signed by David Ashley -S
Date: 2015.11.02 13:36:25 -05'00'

David L. Ashley, Ph.D.
RADM, U.S. Public Health Service
Director
Office of Science

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0010524: General Loose	
Product Name	General Loose
Package Type	Plastic Can
Package Quantity	50 g
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	
SE0010525: General Dry Mint Portion Original Mini	
Product Name	Catch Dry Peppermint Portion Original Mini
Package Type	Plastic Can
Package Quantity	6 g
Portion Count	20 pouches
Portion Mass	300 mg
Portion Length	28 mm
Portion Width	14 mm
Portion Thickness	5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	Peppermint
SE0010526: General Portion Original Large	
Product Name	General Portion Original Large
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	34 mm
Portion Width	18 mm
Portion Thickness	5.5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	None

SE0010532: General Portion White Large	
Product Name	General Portion White Large
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	34 mm
Portion Width	18 mm
Portion Thickness	5.5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	None
SE0010533: General Wintergreen Portion White Large	
Product Name	General Wintergreen Portion White Large
Package Type	Plastic Can
Package Quantity	24 g
Portion Count	24 pouches
Portion Mass	1000 mg
Portion Length	34 mm
Portion Width	18 mm
Portion Thickness	5.5 mm
Tobacco Cut Size[1]	(b) (4)
Characterizing Flavor	Wintergreen

The predicate tobacco products are loose and portioned snus smokeless tobacco products manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

The applicant submitted the SE Reports on June 10, 2014. FDA issued an Advice/Information Request letter (A/I letter) on September 9, 2014 with a response due by November 8, 2014. In response, the applicant submitted an amendment on November 6, 2014 (SE0010735). On February 5, 2015, FDA issued a Preliminary Finding letter, with a response due date of March 7, 2015. The applicant responded to the Preliminary Finding letter on March 6, 2015 (SE0010948). FDA held a teleconference with the applicant on April 1, 2015, to obtain additional information regarding the submitted stability data. FDA held a second teleconference with the applicant on April 16, 2015, to obtain additional information regarding the Environmental Assessment. FDA held a third teleconference with the applicant on April 24, 2015, to obtain additional information about design parameters. In response to the teleconferences, the applicant submitted two amendments (SE0011679 and SE0011711).

Product Name	SE Report	Amendments
General Loose	SE0010524	SE0010735
General Dry Mint Portion Original Mini	SE0010525	SE0010948
General Portion Original Large	SE0010526	SE0011679
General Portion White Large	SE0010532	SE0011687
General Wintergreen Portion White Large	SE0010533	SE0011711

1.3. SCOPE OF REVIEW

This review captures all administrative, compliance, and scientific reviews completed for these SE Reports.

2. REGULATORY REVIEW

Regulatory reviews were completed by Atasi Poddar on June 20, 2014, by Kendric Neely on November 14, 2014, and by Stephanie Redus on March 11, 2015.

The final regulatory reviews conclude that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed reviews to determine whether the applicant established that the predicate tobacco products are grandfathered products (i.e., were commercially marketed as of February 15, 2007). The OCE reviews dated July 1, 2014, conclude that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco products are grandfathered, and, therefore, are eligible predicate tobacco products.

The Office of Compliance and Enforcement (OCE) also completed a review to determine whether the new tobacco products are in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), as required by section 905(j)(1)(A)(i) of the FD&C Act. The applicant submitted labeling in support of these SE Reports, and the submitted labeling included the applicant's proposed modified risk claims (which are the subject of pending MRTPAs). The OCE review dated May 20, 2015, concludes that the new tobacco products are in compliance with the FD&C Act; if, however, FDA does not issue an MRTP order for all modified risk claims in the pending MRTP applications, then the products would be considered in violation of section 903(a)(1) of the FD&C Act.

4. SCIENTIFIC REVIEW

Scientific reviews were completed by the Office of Science (OS) for the following disciplines:

4.1. CHEMISTRY

Chemistry reviews were completed by Shixia Feng on August 13, 2014, and December 17, 2014.

The final chemistry review concludes that the new tobacco products have different characteristics related to product composition compared to the predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The review identified the following significant difference in characteristics related to composition:

- Different tobacco blends

The applicant explained that the key reason for the differences in tobacco blend is to maintain or reduce HPHC levels in the new tobacco products compared to the corresponding predicate tobacco products. This explanation is supported by submitted HPHC data, which do not indicate significant increases in HPHC levels in the new tobacco products compared to those from the corresponding predicate tobacco products (see Section 4.4 of this TPL review). Therefore, the review concludes that the differences in characteristics related to product composition between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a chemistry perspective.

4.2. ENGINEERING

Engineering reviews were completed by Komal Singh on July 29, 2014, January 6, 2015, and May 7, 2015.

The final engineering review concludes that the new tobacco products have different characteristics related to product design compared to the corresponding predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The review identified the following significant differences in characteristics related to design:

- Decrease in package quantity[2] ((b) (4) %) [SE0010524]
- Decrease in moisture (b) (4) %) [SE0010532 and SE0010533]

The moisture decrease is small and, therefore, does not cause the new tobacco products to raise different questions of public health. The decrease in package

[2] Referred to as “can net weight” in the engineering review.

quantity was deferred to the social science reviewer. Therefore, the differences in characteristics related to product design between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from an engineering perspective.

4.3. MICROBIOLOGY

Microbiology reviews were completed by Norma Duran on September 8, 2014, and Almaris Alonso on December 29, 2014, and April 23, 2015.

The final microbiology review concludes that the new tobacco products have different characteristics related to product microbiology compared to the corresponding predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The microbiological characteristics of the new and corresponding predicate tobacco products are very similar. The review only identified the following significant difference in characteristic related to microbiology:

- Increase in shelf life (from (b) (4) weeks to (b) (4) weeks) [SE0010525]

The SE Report includes adequate stability data to demonstrate the increased shelf life. Therefore, the differences in characteristics related to microbiology between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health.

4.4. TOXICOLOGY

Toxicology reviews were completed by Alex Zheng on September 15, 2014, January 15, 2015, and May 6, 2015.

The final toxicology review concludes that there are no significant differences in characteristics related to toxicology of the new and predicate tobacco products in SE0010533 and, therefore, the new tobacco product does not raise different questions of public health from a toxicology perspective. The review identified the following significant difference in characteristics related to toxicology:

- (b)(4) Increase in arsenic and (b)(4) increase in cadmium [SE0010524]
- (b)(4) increase in cadmium and (b)(4) increase in NNN [SE0010525]
- (b)(4) Increase in arsenic, (b)(4) Increase in cadmium, and (b)(4) increase in formaldehyde [SE0010526]
- (b)(4) Increase in arsenic and (b)(4) increase in cadmium [SE0010532]

As explained in the review, while significantly increased, the quantities of these HPHCs in the new tobacco products are low. For example, in SE0010524, there is a (b)(4) increase in cadmium, but the quantity of cadmium in the new tobacco product is only (b) (4) µg/pouch; therefore, the absolute quantity is low. In my

evaluation, I also find that some of these differences are not statistically significant when variability in measurement is taken into account. Therefore, this difference in characteristics related to toxicology between the new and corresponding predicate tobacco product do not cause the new tobacco product to raise different questions of public health from a toxicological perspective.

4.5. SOCIAL SCIENCE

Social science reviews were completed by Amber Koblitz on August 27, 2014, by Alexander Peroskie on December 29, 2014,[3] and by Anh Nguyen on October 29, 2015.

The final social science review concludes that the new tobacco product in SE0010525 has the same characteristics related to consumer perception and use as the predicate tobacco product. The review concludes that the new tobacco products in SE0010524, SE0010526, SE0010532, and SE0010533 have different characteristics related to consumer perception and use compared to the corresponding predicate tobacco products but the differences do not cause the new tobacco products to raise different questions of public health. The review only identified the following significant difference in characteristic related to social science:

- (b) (4) Decrease in package quantity[4] [SE0010524]
- Change in flavor ingredients (without change in or addition of a characterizing flavor) [SE0010526, SE0010532, and SE0010533]

The review states that the decrease in package quantity is small and results in a (b) % decrease in the height of the can, which is so small as to be unlikely to affect consumer perception and use. The review deferred the flavor differences to chemistry to determine whether the flavor differences would change characterizing flavor. Chemistry did not find the flavor differences to change the characterizing flavor, so the ingredient changes are not significant differences. Therefore, the differences in characteristics related to consumer perception and use between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a social science perspective.

The review also evaluated the health information summary for each new tobacco product and determined that it potentially violates section 911 of the FD&C Act. However, upon reconsideration, FDA has determined that the statements provided for this Report which are required in a health information summary pursuant to section 910(a)(4) of the FD&C Act do not constitute modified risk claims. Therefore, the applicant's health information summary for each new tobacco product does not violate section 911.

[3] There was an addendum review completed by Alexander Peroskie on January 29, 2015.
[4] Referred to as "package size" in the social science review.

5. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on August 21, 2015. The FONSI was supported by an environmental assessment prepared by FDA on August 21, 2015.

6. CONCLUSION AND RECOMMENDATION

The following are the key differences in characteristics between the new and predicate tobacco products:

- Different tobacco blends
- (b)(4) % Decrease in package quantity[5]
- (b)(4) % Decrease in moisture[6]
- Increase in shelf life (from (b)(4) weeks to (b)(4) weeks)[7]
- (b)(4) % Increase in arsenic and (b)(4) % increase in cadmium[5]
- (b)(4) % increase in cadmium and (b)(4) % increase in NNN[7]
- (b)(4) % Increase in arsenic, (b)(4) % Increase in cadmium, and (b)(4) % increase in formaldehyde[8]
- (b)(4) % Increase in arsenic and (b)(4) % increase in cadmium[9]

The significant differences in tobacco blend resulted from the applicant's effort to maintain or reduce HPHC levels. In spite of the applicant's effort, the quantities of arsenic, cadmium, formaldehyde, and NNN increased. However, the increases do not cause the new tobacco products to raise different questions of public health because the quantities are low and, therefore, not of toxicological concern. In addition, when variability in measurement is taken into account, some of these differences are not statistically significant. The decrease in moisture is not significant. The decrease in package quantity is small and only decreases the height of the can by (b)(4)%. This small change is unlikely to affect consumer perception and use. The increase in shelf life is supported by stability data submitted in the SE Report. Therefore, the reviews conclude that the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health.

The predicate tobacco products meet statutory requirements because they are grandfathered products (i.e., were commercially marketed in the United States as of February 15, 2007).

All of the new tobacco products are currently in compliance with the FD&C Act. If, however, FDA does not issue an MRTP order, then the new tobacco products would

[5] SE0010524 only
[6] SE0010532 and SE0010533 only
[7] SE0010525 only
[8] SE0010526 only
[9] SE0010532 only

be considered in violation of section 903(a)(1) of the FD&C Act. In addition, all of the scientific reviews conclude that the differences between the new and corresponding predicate tobacco products are such that the new tobacco products do not raise different questions of public health. I concur with the conclusions in the scientific reviews and recommend that SE order letters be issued.

FDA examined the environmental effects of finding these new tobacco products substantially equivalent and made a finding of no significant impact.

SE order letters should be issued for the new tobacco products in SE0010524 – SE0010526 and SE0010532 – SE0010533, as identified on the cover page of this review.