FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review:

SE0001909, SE0001912, and SE0001919

SE0001909: Kayak Fine Cut Wintergreen	
Product Sub-Category	Loose Moist Snuff
Package Type	Plastic can and lid
Package Quantity	1.2 ounces
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Wintergreen
SE0001912: Kayak Long Cut Grape	
Product Sub-Category	Loose Moist Snuff
Package Type	Plastic can and lid
Package Quantity	1.2 ounces
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Grape
SE0001919: Kayak Pouches Wintergreen	
Product Sub-Category	Portioned Moist Snuff
Package Type	Plastic can and lid
Package Quantity	0.82 ounces
Portion Count	15 pouches
Portion Mass	1.6 grams/pouch
Portion Length	35 mm
Portion Width	21 mm
Portion Thickness	6 mm
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Wintergreen
Additional Property	Fine Cut
Common Attributes of SE Reports	
Applicant	Swisher International Inc.
Report Type	Provisional
Product Category	Smokeless Tobacco Products
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Kenneth Taylor -S
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DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Kenneth Taylor -S, 0.9.2342.19200300.100.1.1=12001623932
Date: 2018.10.19 14:32:21 -04'00'

Kenneth M. Taylor, Ph.D.
Chemistry Branch Chief
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 Matthew R. Holman -S
Date: 2018.10.22 09:43:18 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0001909: Kayak Fine Cut Wintergreen	
Product Name	Kayak Fine Cut Wintergreen
Product Sub-Category	Loose Moist Snuff
Package Type	Plastic can and lid
Package Quantity	1.2 ounces
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Wintergreen
SE0001912: Kayak Long Cut Grape	
Product Name	Kayak Long Cut Peach
Product Sub-Category	Loose Moist Snuff
Package Type	Plastic can and lid
Package Quantity	1.2 ounces
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Peach
SE0001919: Kayak Pouches Wintergreen	
Product Name	Silverado Wintergreen Pouches
Product Sub-Category	Portioned Moist Snuff
Package Type	Plastic can and lid
Package Quantity	0.82 ounces
Portion Count	15 pouches
Portion Mass	1.6 grams/pouch
Portion Length	35 mm
Portion Width	21 mm
Portion Thickness	6 mm
Tobacco Cut Size	(b) (4)
Characterizing Flavor	Wintergreen
Additional Property	Fine Cut

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 22, 2011, FDA received three SE Reports (SE0001909, SE0001912 and SE0001919) from Swisher International Inc. (Swisher) and subsequently issued Acknowledgment letters on August 30, 2011. On July 11, 2012, FDA received unsolicited amendments (SE0004677 and SE0004680) for SE0001909 and SE0001912 containing environmental assessments. On January

28, 2013, FDA received an unsolicited amendment (SE0006907) for SE0001919 containing an environmental assessment. On April 29, 2013, FDA issued Advice/Information Request (A/I) letters for all SE Reports. On May 21, 2013 and May 24, 2013, FDA received the applicant's responses to the A/I letters (SE0008598, SE0008612 and SE0008616) for SE0001909, SE0001912 and SE0001919. On September 12, 2013, FDA conducted a telecon to request the applicant confirm the package sizes for all of the SE Reports. On September 16, 2013, FDA received an amendment (SE0009803) containing the requested information. On October 8, 2013 and October 9, 2013, FDA received unsolicited amendments (SE0009887, SE0009890 and SE0009897) for SE0001909, SE0001912 and SE0001919 containing proof of grandfathered status for the predicate products.

On December 9, 2016, FDA issued a Notification letter informing Swisher that scientific review for these SE Reports was expected to begin on January 23, 2017. On January 23, 2017, FDA received an amendment (SE0013844) for all SE Reports in response to the Notification letter. FDA issued a Preliminary Finding (Pfind) letter on April 6, 2017 because the applicant had not uniquely identified the new and predicate tobacco products. On May 5, 2017, FDA received the applicant's response to the Pfind letter (SE0014077). On May 26, 2017, FDA received responses to the Office of Compliance and Enforcement's (OCE's) predicate eligibility request (SE0014119). On September 25, 2017, FDA issued an A/I letter. On October 20, 2017, FDA received the applicant's request for a 90-day extension to respond to the September 25, 2017 A/I letter (SE0014386). On November 2, 2017, FDA issued an Extension Request Granted letter, extending the applicant's time to respond to February 22, 2018. On February 22, 2018, FDA received the applicant's response to the September 25, 2017 A/I letter (SE0014550). On May 3, 2018, FDA issued a Pfind letter. On May 22, 2018, FDA received the applicant's request for an 8-month extension to respond to the Pfind letter (SE0014730). On June 5, 2018, FDA issued an Extension Request Denied letter, denying the 8-month extension request. On June 20, 2018, FDA received the applicant's amendment in response to the May 3, 2018 Pfind letter (SE0014784). The amendment is considered late as it was received by FDA after the due date of response, June 2, 2018, had passed. Because FDA issued the Extension Request Denied letter three days after the Pfind letter response due date, FDA decided to accept the late amendment and include it as part of the next round of review.

Product Name	SE Report	Amendments
Kayak Fine Cut Wintergreen	SE0001909	SE0004677 SE0008598 SE0009803 SE0009887 SE0013844 SE0014077 SE0014119 SE0014386 SE0014550 SE0014730 SE0014784

Product Name	SE Report	Amendments
Kayak Long Cut Grape	SE0001912	SE0004680 SE0008612 SE0009803 SE0009890 SE0013844 SE0014077 SE0014119 SE0014386 SE0014550 SE0014730 SE0014784
Kayak Pouches Wintergreen	SE0001919	SE0006907 SE0008616 SE0009803 SE0009897 SE0013844 SE0014077 SE0014119 SE0014386 SE0014550 SE0014730 SE0014784

1.3. SCOPE OF REVIEW

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

2. REGULATORY REVIEW

Regulatory reviews were completed by Stephanie Durkin on April 29, 2013 and by Jaime Golwalla on September 11, 2018.

The final 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 June 7, 2017 and

June 9, 2017, 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.[2]

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 Youbang Liu on August 4, 2017, April 10, 2018, and August 3, 2018.

The final chemistry review concludes that the new tobacco products have different characteristics related to product chemistry 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 differences:

- SE0001912
  - 68% increase in acetaldehyde
  - 11% increase in NNN

- SE0001919
  - 313% increase in the preservative, (b) (4)
  - 146% increase in NNK

Whether the higher amounts of (b) (4), acetaldehyde, NNN, NNK cause the new tobacco products to raise different questions of public health were deferred to the toxicology review.

Therefore, 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 from a chemistry perspective.

4.2. ENGINEERING

Engineering reviews were completed by James Roche on August 8, 2017, by Rashele Moore on April 10, 2018, and by Drew Katherine on August 3, 2018[3].

The final engineering review did not identify any differences in characteristics between the new and corresponding predicate tobacco products that could cause the new tobacco products to raise different questions of public health from an engineering perspective.

[2]Addendum reviews were completed on August 29, 2018 to include characterizing flavor for the predicate products; the conclusions in these addendum reviews did not differ from that in the original June 7, 2017 and June 9, 2017 reviews.
[3] An addendum to the engineering reviews on October 12, 2018 corrects portion mass target specification and range limits values for SE0001919.

Therefore, 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 related to product engineering.

4.3. MICROBIOLOGY

Microbiology reviews were completed by Win Lin, on August 7, 2017 and by David Craft on April 13, 2018 and August 7, 2018.

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 review identified the following differences:

- SE0001909
  - 11% increase in NNN at beginning of product storage
  - 3% decrease in NNN at end of product storage
  - Greater decrease (28 vs 19%) in NNN during complete product storage time

- SE0001912
  - Increases in preservatives, (b) (4)
  - Removal of (b) (4) as a humectant
  - Increases in humectants, (b) (4)
  - Increases in NNN (11%) and NNK (7%) at beginning of product storage
  - Increases in NNN (5%) and NNK (3%) at end of product storage
  - A 1% decrease in NNN compared to a 4% increase during complete product storage time; greater decrease (9% vs 5%) in NNK

- SE0001919
  - Removal of the preservative, (b) (4)
  - (b) (4) increase in the preservative, (b) (4)
  - (b) (4) decrease in the humectant water
  - Increases in humectants, (b) (4)
  - Increases in NNN (2%) and NNK (7%) at the beginning of product storage
  - Increases in NNN (6%) and NNK (10%) at the end of product storage
  - 2% increase in NNN compared to a decrease of 3% during complete product storage time; lesser decrease (10% vs 12%) in NNK

The new tobacco product in SE0001909 has an 11% increase in NNN at the beginning of product storage time compared to the corresponding predicate product. The increase is not a concern because at the end of storage time, NNN decreased 3% in the new tobacco product and also decreased more (28% vs. 19%) during the complete storage time of (b) (4) in comparison to the corresponding predicate product. The new tobacco products in SE0001912 and SE0001919 showed changes in preservatives and humectants, both of which could potentially affect the microbial growth and affect the accumulation of tobacco specific nitrosamines (TSNAs) in the final tobacco product during storage. For SE0001912, the NNN and NNK levels of the new tobacco product were higher than the corresponding predicate tobacco product at the beginning (11 and 7%, respectively) and end (5 and 3%, respectively) of product storage time.

However, these increases are not a concern because during the complete storage time of (b) (4), the new tobacco product had a 1% decrease in NNN and a 9% decrease in NNK. For SE0001919, the NNN and NNK levels of the new tobacco product were higher than the predicate tobacco product at the beginning (2 and 7%, respectively) and end (6 and 10%, respectively) of product storage time. However, this is not of concern because over the complete storage time of (b) (4), the new tobacco product showed a minor (2%) increase in NNN and a 9% decrease in NNK.

Therefore, 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 from a microbiology perspective.

4.4. TOXICOLOGY

Toxicology reviews were completed by Guy Lagaud on August 11, 2017, April 23, 2018, and August 07, 2018.

The final toxicology review concludes that the new tobacco products have different characteristics related to toxicology 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 differences:

- SE0001909
  - 11% increase in NNN
  - Increase in a permeation enhancer ingredient (b) (4)
- SE0001912
  - Increases of 6%, 28% and 2501% in the respective amounts of (b) (4)
  - 11% increase in NNN
  - 68% increase in acetaldehyde
  - Increase in (b) (4)
  - Increase in (b) (4)
  - Increases in permeation enhancer ingredients (b) (4)
- SE0001919
  - Removal of the preservative (b) (4)
  - 146% increase in NNK
  - 313% increase in the preservative (b) (4)
  - Increase in (b) (4)
  - Increases in permeation enhancer ingredients (b) (4)

The toxicology review determined that the increases in acetaldehyde (SE0001912) and NNN (SE0001909 and SE0001912) and NNK (SE0001919) in the new tobacco products do not present a concern. For acetaldehyde, the amount present in the new tobacco product is 41-fold less than the no-observed-adverse-effect-level (NOEL) for food. Stability studies provided by the

applicant for all of the SE Reports did not show, despite initial increases at the beginning, any significant differences in the amounts of NNN and NNK between the new and predicate tobacco products during the complete storage time to cause different questions of public health. The stability studies and marginal differences in the amounts of NNN and NNK during product storage also show that removal of the preservative (b) (4) is not a concern. The increased amounts of (b) (4) (complex ingredient) in the new tobacco product for SE0001912 are not a concern because these ingredients are still less than average daily intake levels seen in food products. The increases in (b) (4) for the new tobacco products in SE0001912 and SE0001919 are at amounts less than toxicity values for (b) (4) recommended by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and are not a concern. Similarly, the amount of propyl paraben in the new tobacco product for SE0001912 is below published toxicity levels and is not a concern. The very large increase (313%) in another preservative, (b) (4), in the new tobacco product for SE0001919 is less than the NOEL in short term animal studies and is therefore not a concern. Finally, the new tobacco products have increases in several permeation enhancers. The increase in (b) (4) is not a concern because it is present in amounts that are 32-fold less than the lowest level that has been observed for permeation enhancement. Similarly, (b) (4) denatured is not a concern because JECFA has not specified limitations and it is less than concentrations that have been shown to affect NNN permeability. The increase in (b) (4) is offset by the absence of (b) (4), a more effective permeation enhancer, in the new tobacco products compared to the corresponding predicate tobacco products.

Therefore, 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 from a toxicology perspective.

5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(a), issuance of SE orders under section 910(a) of the FD&C Act for these provisional SE Reports is categorically excluded and, therefore, normally does not require the preparation of an environmental assessment (EA) or an environmental impact statement. FDA has considered whether there are extraordinary circumstances that would require the preparation of an EA and has determined that none exist.

6. CONCLUSION AND RECOMMENDATION

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

- SE0001909
  - Increases in (b) (4), a permeation enhancer
  - 11% increase in NNN at beginning of product storage
  - 3% decrease in NNN at end of product storage
  - Greater decrease (28 vs 19%) in NNN during complete product storage time

- SE0001912
  - Increases of 6%, 28% and 2501% in the respective amounts of (b) (4),

(b) (4) (complex ingredient)
- Increases in NNN (11%) and NNK (7%) at beginning of product storage
- Increases in NNN (5%) and NNK (3%) at end of product storage
- 1% decrease in NNN (vs. 4.4% increase) during complete product storage time.
- Greater decrease (9% vs 5%) in NNK during complete product storage
- 68% increase in acetaldehyde
- Increase in (b) (4)
- Increases in preservatives (b) (4)
- Increases in permeation enhancer ingredients (b) (4)
- Removal of (b) (4) as a humectant
- Increases in the humectants (b) (4)

- SE0001919
  - Removal of (b) (4) as a preservative
  - 146% increase in NNK
  - Increases in NNN (2%) and NNK (7%) at the beginning of product storage
  - Increases in NNN (6%) and NNK (10%) at the end of product storage
  - 2% increase in NNN compared to a decrease of 3% during complete product storage time
  - A comparable decrease (10% vs. 12%) in NNK during complete product storage
  - 313% increase in (b) (4) as a preservative
  - Increase in (b) (4)
  - Increases in permeation enhancer ingredients (b) (4)
  - (b) (4) decrease in water as a humectant
  - Increases in humectants (b) (4)

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. Both microbiology and toxicology reviews conclude that based on stability studies, the differences in NNN and NNK between the new and corresponding predicate tobacco products are minor and do not cause a concern. Similarly, the increase in acetaldehyde in the new product is not a concern because the amount present is 41-fold less than the NOEL for food. The increased amounts of (b) (4) in the new tobacco product for SE0001912 are not a concern because the amounts of these ingredients are still less than average daily intake levels seen in food products. The increases in (b) (4) for the new tobacco products in SE0001912 and SE0001919 are at amounts less than toxicity values for (b) (4) recommended by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and are not a concern. Similarly, the amount of (b) (4) in the new tobacco product for SE0001912 is below published toxicity levels and is not a concern. Finally, the new tobacco products have increases in several permeation enhancers. The increase in (b) (4) is not a concern because it is present in amounts that are 32-fold less than the lowest level that has been observed for permeation enhancement. Similarly, (b) (4) is not a concern because JECFA has not specified limitations and it less than concentrations that have been shown to affect NNN permeability. The increase in (b) (4) is offset by the absence of (b) (4), a more effective permeation enhancer, in the new tobacco products compared to the corresponding predicate tobacco products. There are increases in some humectants, but these are offset by removal of other humectants. As noted in

the microbiology review, changes in preservatives and humectants can affect microbial activity. However, based on TSNA levels measured from the stability studies, microbial activity appears to be unaffected by the change in preservatives and humectants of the new tobacco products. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new tobacco products to raise different questions of public health.

The predicate tobacco products meet statutory requirements because it was determined that they are grandfathered products (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

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 these reviews and recommend that SE order letters be issued.

Because the proposed action is issuing SE orders for the provisional SE Reports, it is a class of action that is categorically excluded under 21 CFR 25.35(a). FDA has considered whether there are extraordinary circumstances that would require the preparation of an environmental assessment and has determined that none exist. Therefore, the proposed action does not require preparation of an environmental assessment or an environmental impact statement.

SE order letters should be issued for the new tobacco products in SE0001909, SE0001912, and SE0001919, as identified on the cover page of this review.