FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0000499

SE0000499: Husky Long Cut Wintergreen	
Package Type	Plastic Can and Lid
Package Quantity	34.02 grams (g)
Tobacco Cut Size	(b) (4) [redacted]
Characterizing Flavor	Wintergreen
Common Attributes of SE Reports	
Applicant	U.S. Smokeless Tobacco Company LLC
Report Type	Provisional
Product Category	Smokeless Tobacco Product
Product Sub-Category	Loose Moist Snuff
Recommendation	
Issue a Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

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Date: 2020.02.19 16:36:03 -05'00'

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: 2020.02.19 17:19:50 -05'00'

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

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco products:

SE0000499: Husky Long Cut Wintergreen	
Product Name	Husky Long Cut Wintergreen
Package Type	Plastic Can and Lid
Package Quantity	34.02 g
Tobacco Cut Size	(b) (4) [redacted]
Characterizing Flavor	Wintergreen
Product Name	Rooster Long Cut Wintergreen
Package Type	Plastic Can and Lid
Package Quantity	34.02 g
Tobacco Cut Size	(b) (4) [redacted]
Characterizing Flavor	Wintergreen

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 18, 2011, FDA received a SE Report from Altria Client Services (ALCS) on behalf of U.S. Smokeless Tobacco Company, LLC (USSTC). On October 5, 2011, FDA issued an Acknowledgement letter. On November 4, 2011, the applicant submitted an informational update on the SE Report (SE0003872). On January 2, 2013, FDA issued an Advice/Information (A/I) Request letter. On January 25, 2013 and May 29, 2013, FDA received the applicant's responses to the A/I Request letter (SE0006739 and SE0008691, respectively). On January 22, 2018, FDA issued a Notification letter to inform the applicant that scientific review of the SE Report would begin on March 8, 2018. On March 7, 2018, FDA received an amendment providing information for the SE Report (SE00014568). On May 31, 2018, FDA issued the applicant an A/I Request letter. On June 15, 2018, FDA received the applicant's request for an extension to respond to the A/I Request letter (SE0014782). On July 16, 2018, FDA issued an Extension Granted letter with a response due date of February 1, 2019. On January 25, 2019, FDA received the applicant's response to the A/I Request letter (SE0015070). On April 18, 2019, FDA issued a Preliminary Finding (PFind) letter. On June 28, 2019, FDA received the applicant's response to the PFind letter (SE0015276).

Product Name	SE Report	Amendments
Husky Long Cut Wintergreen	SE0000499	SE0003872 SE0006739 SE0008691 SE0014568 SE0014782 SE0015070 SE0015276

1.3. SCOPE OF REVIEW

This review captures all regulatory, compliance, and scientific review completed for this SE Report.

2. REGULATORY REVIEW

Regulatory reviews were completed by Cathryn Lee on October 4, 2011, Tamu Monroe on January 2, 2013, Atasi Poddar on March 19, 2013 and by Ryan Nguy on January 10, 2020.

The final review concludes that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the applicant established that the predicate tobacco product is a grandfathered product (i.e., was commercially marketed in the United States other than exclusively in test markets as of February 15, 2007). The OCE review dated April 6, 2018, concludes that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco product is grandfathered and, therefore, is an eligible predicate tobacco product.

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 Jiu Ai on April 25, 2018 and March 11, 2019[1].

[1] Amended on December 18, 2019 to evaluate HPHC data using an updated Two One-Sided T-test (TOST), which is a statistical tool that calculates important analytical differences using the Horwitz-Thompson equation. The mean range of a TOST analysis is a measure of statistical probability that differences in a mean range of tested values are analytically significant. An equivalence margin at a 75% confidence interval reduces the number of inconclusive results, which default to be considered as not analytically equivalent.

The final chemistry review concludes that the new tobacco product has different characteristics related to product chemistry compared to the predicate tobacco products, but the differences does not cause the new tobacco product to raise different questions of public health. The review identified the following differences:

- Tobacco blend:
  - 3.4% decrease (vs. Husky Long Cut Wintergreen) and 4.9% increase (vs. Rooster Long Cut Wintergreen) in total tobacco
  - [redacted] mg/g increase in [redacted] tobacco
  - 2.4% decrease (vs. Husky Long Cut Wintergreen) and 5.3% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
  - 5.1% decrease (vs. Husky Long Cut Wintergreen) and 3.3% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
  - 4.4% decrease (vs. Husky Long Cut Wintergreen) and 3.8% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
- Non-Tobacco ingredients:
  - Removal of [redacted] (vs. Rooster Long Cut Wintergreen)
  - 79% decrease in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 79% decrease in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 15% increase in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 42% decrease (vs. Husky Long Cut Wintergreen) and 46% increase (vs. Rooster Long Cut Wintergreen) in [redacted]
- Addition of [redacted] mg/g)
- Addition of [redacted] mg/g)
- Addition of [redacted] mg/g)
- 24% increase in free nicotine (Husky Long Cut Wintergreen)

The new tobacco product contains [redacted] which the predicate products do not. Also, compared to the Rooster Long Cut Wintergreen predicate product, the total tobacco in the new tobacco product is increased 5%. The changes in tobacco blend may affect harmful and potentially harmful constituents (HPHCs) amounts. There are also non-tobacco ingredient differences. The increases in [redacted] and additions of [redacted] are not anticipated to affect HPHCs. The chemistry review concludes that nicotine, arsenic, cadmium, benzo-α-pyrene, acetaldehyde, crotonaldehyde, formaldehyde, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and N-nitrosonornicotine (NNN) are analytically equivalent between the new and predicate tobacco products. Additionally, the new tobacco product is calculated to have a 24% increase in free nicotine compared to the corresponding predicate tobacco product, Husky Long Cut Wintergreen, due to an increase in pH from (b)(4). However, the nicotine dissolution rate between the new and Husky Long Cut Wintergreen are similar, indicating that the pH and free nicotine difference is not a concern. Also, the similarity in dissolution rates between both Husky Long Cut Wintergreen new and predicate tobacco products demonstrates that the cut size difference between these products is not a concern.

Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health from a chemistry perspective.

4.2. ENGINEERING

Engineering reviews were completed by Raymond L. Williamson on April 24, 2018 and on March 19, 2019[2].

The final engineering review concludes that the new tobacco product has different characteristics related to product engineering compared to the predicate tobacco products, but the differences do not cause the new tobacco product to raise different questions of public health. The review identified the following difference:

- (b) (4) increase in tobacco cut size (CPI) (vs. Husky Long Cut Wintergreen)

Differences in tobacco cut size may alter the particle surface area and accessibility of saliva to the surfaces of the tobacco, thereby affecting the amount and rate of constituents released from the product. To address this, the applicant provided dissolution data for nicotine. The engineering review deferred nicotine release rate data to the chemistry review.

Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health from an engineering perspective.

4.3. MICROBIOLOGY

Microbiology reviews were completed by David L. Craft on April 25, 2018 and by Almaris Alonso on March 26, 2019.

The final microbiology review concludes that the new tobacco product has different characteristics related to product microbiology compared to the predicate tobacco products, but

[2] Amended on February 19, 2020.

the differences does not cause the new tobacco product to raise different questions of public health. The review identified the following differences:

- Minor increases (≤5%) in pH, OV%, and a_w[3] at (b)(4) of product storage[4]
- Decreases in NNN (≤37%) and NNK (≤58%) at (b)(4) of product storage (vs. Husky Long Cut Wintergreen)
- 38% decrease in tobacco-specific nitrosamines (TSNAs) at 2, 12 and 22 weeks (vs. Husky Long Cut Wintergreen)[5]
- Increases in (b) (4) levels (≤11%) (b)(4) weeks of product storage (vs. Rooster Long Cut Wintergreen)
- Addition of (b) (4) as a preservative
- Increases in Total Aerobic Microbial counts (TAMC) during product storage (vs. Rooster Long Cut Wintergreen)
- Decreases (≤60%) in TAMC at (b)(4) of product storage (vs. Husky Long Cut Wintergreen)

The applicant provided stability data at (b)(4) storage intervals for the new and two predicate products (Husky Long Cut Wintergreen and Rooster Long Cut Wintergreen). The decreases in NNN, NNK and total TSNAs compared to Husky Long Cut Wintergreen are favorable and do not cause concerns. The 11% increase in (b) (4) levels of the new tobacco product compared to Rooster Long Cut Wintergreen is not a concern because (b) (4) which is an intermediate in the biosynthetic pathway of TSNAs, is below detection limits in the new and both predicate tobacco products. The lack of detectable (b) (4) makes microbiological conversion of (b) (4) to (b) (4) in the new tobacco product unlikely, therefore preventing unstable NNN, NNK and TSNA levels in the final product. Similarly, that (b) (4) content in the new product is below limit of detection also demonstrates that the higher TAMC values observed in the new product when compared to the predicate product, Rooster Long Cut Wintergreen is inconsequential because it demonstrates that the potential for unstable microbiological activity should not occur. Moreover, the new tobacco product contains (b) (4) which is a preservative that is used to reduced TSNA formation. (b) (4) decreased just 2% during the tested product storage of (b)(4). The microbiology relevant parameters of pH, OV%, a_w, NNN, NNK, TSNAs levels, (b) (4) is essentially stable during this period. However, due to the toxic nature of (b) (4) evaluation is deferred to Toxicology.

Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health from a microbiology perspective.

4.4. TOXICOLOGY

Toxicology reviews were completed by Lynn Crosby on May 10, 2018 and April 01, 2019; and by Thomas Hill on November 19, 2019.

[3] Water activity.
[4] Table 3 of the microbiology review indicates that pH, OV%, and a_w decrease overall during storage time.
[5] The microbiology review dated March 26, 2019 incorrectly indicates that total TSNAs increase in the Conclusion, Section 3.1. Table 5 of the review shows that TSNAs decreases 38% in the new tobacco product.

The final toxicology review concludes that the new tobacco product has different characteristics related to toxicology compared to the predicate tobacco products, but the differences does not cause the new tobacco product to raise different questions of public health. The review identified the following differences:

- Addition of [redacted] mg/g of product
- Decreased [redacted] (4.4%), [redacted] (5.0%), and [redacted] (2.4%) (vs. Husky Long Cut Wintergreen)
- Increases in [redacted] (3.8%), [redacted] (3.3%), and [redacted] (5.3%) tobaccos (vs. Rooster Long Cut Wintergreen)
- Addition of [redacted] mg/g)
- Addition of [redacted] mg/g of product
- Decrease ([redacted] mg/g product) or increase ([redacted] mg/g product) in [redacted] (from [redacted] compared to Husky Long Cut Wintergreen or Rooster Long Cut Wintergreen, respectively.

The toxicology review notes that HPHCs are analytically equivalent between the new and predicate tobacco products and therefore do not cause concerns. With respect to [redacted] the toxicology determined that, based on a 1 can per day consumption, the exposure is below tolerable daily intake (TDI) and chronic population adjusted dose (cPAD) limits.

Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health from a toxicology perspective.

5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(a), issuance of an SE order under section 910(a) of the FD&C Act for this provisional SE Report (SE0000499) 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 predicate tobacco products:

- Tobacco blend:
  - 3.4% decrease (vs. Husky Long Cut Wintergreen) and 4.9% increase (vs. Rooster Long Cut Wintergreen) in [redacted]
  - 4 mg/g increase in [redacted] tobacco
  - 2.4% decrease (vs. Husky Long Cut Wintergreen) and 5.3% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
  - 5.1% decrease (vs. Husky Long Cut Wintergreen) and 3.3% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
  - 4.4% decrease (vs. Husky Long Cut Wintergreen) and 3.8% increase (vs. Rooster Long Cut Wintergreen) in [redacted] tobacco
- Non-Tobacco ingredients:
  - Removal of [redacted] (vs. Rooster Long Cut Wintergreen)
  - 79% decrease in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 79% decrease in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 15% increase in [redacted] (vs. Rooster Long Cut Wintergreen)
  - 42% decrease (vs. Husky Long Cut Wintergreen) and 46% increase (vs. Rooster Long Cut Wintergreen) in [redacted]
- Addition of [redacted] mg/g) as a preservative
- Addition of [redacted] mg/g)
- Addition of [redacted] mg/g)
- 24% increase in free nicotine (vs. Husky Long Cut Wintergreen)
- 22% increase in tobacco cut size (CPI) (vs. Husky Long Cut Wintergreen)
- Decreases in NNN (<37%) and NNK (<58%) at (b)(4) of product storage (vs. Husky Long Cut Wintergreen)
- 38% decrease in TSNAs at (b)(4) (vs. Husky Long Cut Wintergreen)
- Increases in [redacted] level (<11%) at each timepoint tested during storage (vs. Rooster Long Cut Wintergreen)
- Increases in TAMC during product storage (vs. Rooster Long Cut Wintergreen)
- Decreases (<60%) TAMC (b)(4) of product storage (vs. Husky Long Cut Wintergreen)

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. Tested HPHCs are analytically equivalent between the new and both predicate tobacco products, which demonstrate that the tobacco blend changes do not cause concerns. Additionally, the increase in free nicotine, due to the increase in pH, and change in tobacco cut size, does not appear to be a concern based on the similar dissolution profiles of the new tobacco product with the Husky Long Cut Wintergreen predicate. Stability measurements at (b)(4) storage demonstrate that the pH, OV%, a_w, NNN, NNK, TSNAs levels, and [redacted] are essentially stable during this period in the new tobacco product. This indicates that microbial activity is not a concern. The new tobacco product contains [redacted] as a preservative. Even with the added [redacted], anticipated use of [redacted] per day of the new tobacco product the amount of [redacted] consumed is less than TDI and cPAD limits. Therefore, the differences in characteristics between the new and predicate products do not cause the new tobacco product to raise different questions of public health.

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

Because the proposed action is issuing an SE order for the provisional SE Report, 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.

An SE order letter should be issued for the new tobacco product in SE0000499, as identified on the cover page of this review.