FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0015402

SE0015402: Copenhagen Long Cut Special Wintergreen	
Package Type	Plastic Can with Metal Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) Cuts Per Inch (CPI)
Characterizing Flavor	Wintergreen
Additional Property	Long Cut
Common Attributes of SE Reports	
Applicant	U.S. Smokeless Tobacco Company LLC
Report Type	Regular
Product Category	Smokeless Tobacco Product
Product Sub-Category	Loose Moist Snuff
Recommendation	
Issue a Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Digitally signed by Samantha Spindel -S3
Date: 2020.02.20 11:05:59 -05'00'

Samantha Spindel, Ph.D., M.Eng.
CDR, US Public Health Service
Engineering 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: 2020.03.03 14:03:06 -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 product:

SE0015402: Copenhagen Long Cut Special Wintergreen	
Product Name	Copenhagen Long Cut Smooth Wintergreen
Package Type	Plastic Can with Metal Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) CPI
Characterizing Flavor	Wintergreen
Additional Property	Long Cut

The predicate tobacco product is a loose moist snuff smokeless tobacco product manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On August 16, 2019, FDA received an SE Report from Altria Client Services LLC on behalf of U.S. Smokeless Tobacco Company LLC. On August 22, 2019, FDA issued an Acknowledgment letter.

On November 7, 2019, FDA issued a Deficiency letter with a response due date of May 5, 2020. On December 5, 2019, FDA received the response to the Deficiency letter (SE0015591).

Product Name	SE Report	Amendment
Copenhagen Long Cut Special Wintergreen	SE0015402	SE0015591

1.3. SCOPE OF REVIEW

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

2. REGULATORY REVIEW

A regulatory review was completed by Iqra Javaid on August 22, 2019.

The review concludes that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The predicate tobacco product in SE0015402 was determined to be substantially equivalent by FDA under SE0014987. Therefore, the predicate tobacco product is an eligible predicate tobacco product.

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the new tobacco product is in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act) (see section 910(a)(2)(A)(i)(II) of the FD&C Act). The OCE review dated February 4, 2020, concludes that the new tobacco product is in compliance with the FD&C Act.

4. SCIENTIFIC REVIEW

A scientific review was completed by the Office of Science (OS) for the following disciplines:

4.1. CHEMISTRY

Chemistry reviews were completed by Jason Hsieh on October 10, 2019 and January 28, 2020.

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

- Tobacco blend
  - ↓ 10% ([redacted] mg/g) total tobacco
  - ↓ 10% [redacted] [↓ [redacted] mg/g] and (b)(4) [↓ [redacted] mg/g])
  - ↓ 10% [redacted] [↓ [redacted] mg/g] and (b)(4) [↓ [redacted] mg/g])
  - ↓ 10% [redacted] ((b)(4) only [↓ [redacted] mg/g])
  - ↓ 3% [redacted] (↓ [redacted] mg/g)
- Ingredients other than tobacco
  - ↓ 9% [redacted] (↓ [redacted] mg/g)
  - ↑ 4% [redacted] as %OV ([redacted] mg/g)
  - Deletion of [redacted]
  - Flavors:
    - ↓ 10% [redacted] mg/g)
    - ↓ 10% [redacted] mg/g)
    - Presence of [redacted] mg/g)
  - pH Adjusters:
    - ↓ 3% [redacted] mg/g)
    - ↓ 10% [redacted] mg/g)
  - Binders:
    - Addition of [redacted] mg/g)
    - ↑ 25% [redacted] mg/g)
    - ↑ 25% [redacted] mg/g)
- Harmful and Potentially Harmful Constituents (HPHCs)
  - ↓ 7% Total nicotine (0.76 mg/g)
  - ↓ 8% Cadmium (49 ng/g)
  - ↓ 6% Arsenic (8 ng/g)
  - ↓ 9% Benzo[a]pyrene (B[a]P) (3.4 ng/g)
  - ↓ 6% Acetaldehyde (0.24 µg/g)
  - ↓ 6% Formaldehyde (0.036 µg/g)
  - ↓ 13% N-Nitrosonornicotine (NNN) (177 ng/g)

- ↓ 15% 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (68 ng/g)

The new tobacco product has a 10% decrease in the total amount of tobacco and a 3% decrease in the [redacted] tobacco component but contains the same tobacco blend composition (i.e., the relative ratios of the tobacco blends remain the same) as the predicate tobacco product. A lower amount of total tobacco in the new tobacco product may result in lower HPHC quantities; therefore, the tobacco blend differences do not cause the new tobacco product to raise different questions of public health. The new tobacco product contains a lower amount of tobacco additives ([redacted] flavor) and lower amount of pH adjusters ([redacted] compared to the predicate tobacco product. Lower amounts of these ingredients in the new tobacco product as compared to the predicate tobacco product do not cause the new tobacco product to raise different questions of public health.

The applicant submitted HPHC data to support the changes in ingredients. All HPHCs were determined to be analytically nonequivalent, except free nicotine, when comparing the new and predicate tobacco products. However, all analytically nonequivalent HPHCs were lower in quantity (total nicotine, cadmium, arsenic, B[a]P, acetaldehyde, formaldehyde, NNN, NNK). The applicant has provided adequate information on HPHC test methods. Therefore, the differences in HPHCs do not cause the new tobacco product to raise different questions of public health from a chemistry perspective. The new tobacco product contains a higher amount of tobacco binders [redacted] and addition of [redacted] compared to the predicate tobacco product. The dissolution testing demonstrates that nicotine dissolution profiles of the new and predicate products were statistically equivalent [redacted] Therefore, the increase in binders does not cause the new tobacco product to raise different questions of public health.

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

An engineering review was completed by Rashele Moore on October 11, 2019.

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

- 18% decrease in tobacco cut size
- 24% increase in average tobacco particle size

The tobacco cut size decreases [redacted] in the new tobacco product. The applicant did not provide range limits for tobacco cut size but explained the manufacturing process for the new and predicate tobacco products. The manufacturing process and tobacco cut size differ for the new and predicate products; the change in tobacco cut size may alter the particle surface area

and accessibility of saliva to get to the surfaces of the tobacco, thereby affecting the amount and rate of constituents released from the product.

A decrease in tobacco cut size and an increase in the average mean particle size may affect the dissolution rate. Dissolution rate and constituent release data can help demonstrate that these changes do not cause the new tobacco product to raise different questions of public health. The evaluation of dissolution rate/constituent release data provided by the applicant was deferred to chemistry (see section 4.1).

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

A microbiology review was completed by Almaris Alonso Claudio on October 3, 2019.

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

- Change in overall duration of (b) (4) days)
- 140% increase in total aerobic microbial counts (TAMC) at (b)(4) storage time point when assessed in TN0 culture medium
- 7 - 58% increases in TAMC at each storage time point when assessed in TSA SB culture medium

The new tobacco product differs from the predicate tobacco product in the overall duration of the (b) (4) process, which could potentially affect microbial activity and product stability over the storage time of the product. The applicant adequately addressed this concern by providing stability data measured over the complete storage time of the new and predicate tobacco products. The new tobacco product showed increases in microbial counts (at week (b)(4) [140%] in TN0; and all timepoints throughout storage (7% - 58%) in TSA SB) compared to the predicate tobacco product. These increases in TAMC of the new tobacco product could be of concern because microbial-mediated reactions play a key role in the tobacco-specific nitrosamine (TSNA) levels of the final tobacco product during product storage. However, the new tobacco product showed lower levels of NNN (≤ 17%), NNK (≤20%), and total TSNAs (≤15%) compared to the predicate tobacco product at all storage timepoints. Therefore, the change in duration of (b) (4) and the increases in TAMC of the new tobacco product compared to the predicate tobacco product are not of 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 microbiology perspective.

4.4. TOXICOLOGY

A toxicology review was completed by Chad N. Brocker on October 9, 2019.

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

- Decrease in overall total target tobacco weight ([redacted] mg/g product; ↓10.2%)
- Increase or addition of three binder ingredients:
  - [redacted] mg/g product; added)
  - [redacted] mg/g product; ↑25%)
  - [redacted] mg/g product; ↑25%)
- Levels of 11 tobacco ingredients are reduced in the new tobacco product
- [redacted] is removed from the interior lid coating of the container closure system
- Decrease in all eight reported HPHC levels

Ingredient changes were identified in the new tobacco product, such as three [redacted] ingredients that were increased or added to the tobacco component of the new tobacco product, but oral exposure to these binders does not cause the new tobacco product to raise different questions of public health from a toxicological perspective. Reductions in total tobacco content and reductions in the amount of ingredients in the new tobacco product as compared to the predicate tobacco product do not cause the new tobacco product to raise different questions of public health from a toxicological perspective. Removal of an (b)(4) component from the interior lid coating could increase tobacco product exposure to leachate from the underlying tin-plated steel, leading to possible user exposure to the leachate. However, tin has poor bioavailability and ingestion poses no serious health risks. Therefore, elimination of this component from the lid coating does not raise different questions of public health from a toxicological perspective. Although ingredient and tobacco blend changes can affect HPHC levels, all reported HPHCs were lower in the new tobacco product when compared to the predicate tobacco product.

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

Environmental reviews were completed by Thomas Creaven on September 27, 2019, November 4, 2019, and January 16, 2020.

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on February 3, 2020. The FONSI was supported by an environmental assessment prepared by FDA on February 3, 2020.

6. CONCLUSION AND RECOMMENDATION

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

- Tobacco:
  - ↓ 10% (b) (4) mg/g) total tobacco
  - 18% decrease in tobacco cut size
  - 24% increase in average tobacco particle size
  - ↓ 10% (b) (4) mg/g] and (b) (4) mg/g])
  - ↓ 10% (b) (4) mg/g] and (b) (4) mg/g])
  - ↓ 10% (b) (4) mg/g])
  - ↓ 3% (b) (4) mg/g)
- Ingredients other than tobacco
  - ↓ 9%s (b) (4) mg/g)
  - ↑ 4% (b) (4) mg/g)
  - Flavors:
    - ↓ 10% (b) (4) mg/g)
    - ↓ 10% (b) (4) mg/g)
    - Presence of (b) (4) mg/g)
  - pH
    - ↓ 3% (b) (4) mg/g)
    - ↓ 10% (b) (4) mg/g)
  - Binders:
    - Addition of (b) (4) mg/g)
    - ↑ 25% (b) (4) mg/g)
    - ↑ 25% (b) (4) mg/g)
- HPHCs
  - ↓ 7% Total nicotine (0.76 mg/g)
  - ↓ 8% Cadmium (49 ng/g)
  - ↓ 6% Arsenic (8 ng/g)
  - ↓ 9% B[a]P (3.4 ng/g)
  - ↓ 6% Acetaldehyde (0.24 µg/g)
  - ↓ 6% Formaldehyde (0.036 µg/g)
  - ↓ 13% NNN (177 ng/g)
  - ↓ 15% NNK (68 ng/g)

- Change in overall duration of (b) (4))
- 140% increase in TAMC at (b) (4) time point when assessed in TN0 culture medium
- 7 - 58% increases in TAMC at each storage time point when assessed in TSA SB culture medium
- (b) (4) is removed from the interior lid coating of the container closure system

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. The new tobacco product contains the same tobacco blend composition and a lower total amount of tobacco as compared to the predicate

tobacco product. The new tobacco product contains a lower amount of tobacco additives [redacted] compared to the predicate tobacco product. These changes are expected to result in lower quantities of HPHCs and data submitted by the applicant demonstrates that HPHC yields are lower in the new tobacco product compared to the predicate tobacco product. Therefore, these changes do not cause the new tobacco product to raise different questions of public health.

The new tobacco product contains a higher amount of tobacco binders [redacted] addition of [redacted], and lower amount of pH adjusters [redacted] compared to the predicate tobacco product. Changes in the pH additives and the addition of binders in the new tobacco product compared to the predicate tobacco product can affect the release rate and total nicotine released from the product. In addition, a decrease in tobacco cut size and an increase in average tobacco particle size in the new tobacco product as compared to the predicate tobacco product may affect the dissolution rate/constituent release. Dissolution data was evaluated and demonstrates nicotine dissolution profiles of the new and predicate tobacco products are statistically equivalent [redacted] Therefore, these differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

Changes in the overall duration of [redacted] and levels of TAMC at various time points were observed, which can affect microbial activity and product stability. However, the new tobacco product showed lower levels of NNK, NNK, and total TSNAs compared to the predicate tobacco product at all storage timepoints. In addition, although changes were identified in the new tobacco product as compared to the predicate tobacco product (reductions in total tobacco content, ingredient changes, and removal of an (b)(4) from the interior lid coating), none of these changes were of toxicological concern. Therefore, these differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

Where an applicant supports a showing of SE by comparing the new tobacco product to a tobacco product that FDA previously found SE, in order to issue an SE order, FDA must find that the new tobacco product is substantially equivalent to a tobacco product commercially marketed in the United States as of February 15, 2007 (see section 910(a)(2)(A)(i)(I) of the FD&C Act).

The predicate tobacco product in SE0015402 was previously determined to be substantially equivalent by FDA under SE0014987. The predicate tobacco product in SE0014987 was previously determined to be substantially equivalent by FDA under SE0014132. The predicate tobacco product in SE0014132 is a grandfathered (GF) tobacco product; the original grandfathered product was Rooster Long Cut Wintergreen (GF1200066). Therefore, comparison of the new tobacco product to the grandfathered product (Rooster Long Cut Wintergreen, GF1200066, in SE0014132) reveals that the new tobacco product has the following differences in characteristics from Rooster Long Cut Wintergreen, the grandfathered tobacco product:

- Lower total tobacco
- Addition of trace quantities of lid coatings
  - [redacted]
  - [redacted]
- 18% decrease in tobacco cut size

- 24% increase in average tobacco particle size
- Change in container closure system (plastic can with metal lid vs plastic can with plastic lid)
- Changes in composition of (b) (4) tobacco resulting in replacement of (b) (4) (b) (4) mg/g), addition of (b) (4) mg/g) and addition of (b) (4) (b) (4) mg/g)
- Change in overall duration of (b) (4)

The differences in container closure system and addition of (b) (4), a lid coating ingredient, listed above are the same differences in characteristics identified for the new and grandfathered tobacco products in SE0014132. Therefore, these differences do not cause the new tobacco product in SE0015402 to raise different questions of public health. The differences in the composition of the (b) (4) tobacco listed above are the same differences in characteristics identified for the new and predicate tobacco products in SE0014987. Therefore, these differences do not cause the new tobacco product in SE0015402 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in total tobacco, tobacco cut size, average tobacco particle size, addition of (b) (4), and change in duration of (b) (4) between the new tobacco product in SE0015402 and the grandfathered tobacco product do not cause the new tobacco product to raise different questions of public health. Therefore, whether comparing the new tobacco product in SE0015402 to the predicate or grandfathered tobacco products, the new tobacco product does not raise different questions of public health.

The new tobacco product is currently in compliance with the FD&C Act. In addition, all of the scientific reviews conclude that the differences between the new and predicate tobacco products are such that the new tobacco product does not raise different questions of public health. I concur with these reviews and recommend that an SE order letter be issued.

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

An SE order letter should be issued for the new tobacco product in SE0015402, as identified on the cover page of this review.