

Technical Project Lead (TPL) Review: SE0015469

SE0015469: Copenhagen Long Cut Select Wintergreen	
Package Type	Plastic Can and Metal Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) Cuts per Inch (CPI)
Characterizing Flavor	Wintergreen
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: 2020.03.04 13:00:17 -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: 2020.03.04 14:36:23 -05'00'

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

TABLE OF CONTENTS

1. BACKGROUND3

 1.1. PREDICATE TOBACCO PRODUCT 3

 1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW..... 3

 1.3. SCOPE OF REVIEW..... 3

2. REGULATORY REVIEW3

3. COMPLIANCE REVIEW3

4. SCIENTIFIC REVIEW4

 4.1. CHEMISTRY..... 4

 4.2. ENGINEERING 5

 4.3. MICROBIOLOGY 6

 4.4. TOXICOLOGY..... 7

5. ENVIRONMENTAL DECISION.....7

6. CONCLUSION AND RECOMMENDATION7

1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco product:

SE0015469: Copenhagen Long Cut Select Wintergreen	
Product Name	Copenhagen Long Cut Smooth Wintergreen
Package Type	Plastic Can and Metal Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) CPI
Characterizing Flavor	Wintergreen

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 September 12, 2019, FDA received SE0015469 from Altria Client Services LLC, submitted on behalf of U.S. Smokeless Tobacco Company LLC (USSTC). FDA issued an Acknowledgement letter on September 18, 2019. FDA issued a Deficiency letter on November 15, 2019. FDA received the applicant’s response to the Deficiency letter on December 5, 2019 (SE0015592).

Product Name	SE Report	Amendments
Copenhagen Long Cut Select Wintergreen	SE0015469	SE0015592

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 Jessica Kiser on September 18, 2019.

The review concludes that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The predicate tobacco product in SE0015469 was previously determined to be substantially equivalent by FDA as shown in the table below. Therefore, the predicate tobacco product is an eligible predicate tobacco product.

SE Report	Predicate Tobacco Product	Predicate Tobacco Product Found SE Under:	Date
SE0015469	Copenhagen Long Cut Smooth Wintergreen	SE0014987 ¹	February 26, 2019

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 28, 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 Selena Russell on November 01, 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% less (b) (4), 3% less (b) (4) (no change in (b) (4) composition), and 10% (33 mg/g) less total tobacco
- Ingredients: Addition of (b) (4) 25% more (b) (4) and (b) (4) 10% less (b) (4) 10% less (b) (4) 10% less (b) (4) and (b) (4) 10% less (b) (4) 10% less (b) (4) 3% less (b) (4) and 9% less (b) (4)
- Container-closure system: removal of (b) (4)
- 9% less total nicotine

The new tobacco product has less total tobacco and lower amounts of individual tobacco types, compared to the predicate tobacco product, which does not cause the new product to raise different questions of public health. The new tobacco product also has changes in many flavor ingredients and binders, but also has the addition of (b) (4) to the new tobacco product compared to the predicate tobacco product. For example, the new tobacco product has more binders than the predicate tobacco product. The addition of (b) (4) and differences in flavor ingredients does not alter the characterizing flavor, wintergreen, between the new and

¹ The predicate product in SE0014987 was found SE in SE0014132 on May 24, 2018. The predicate product in SE0014132 is Rooster Long Cut Wintergreen, which is a grandfathered tobacco product under GF1200066.

predicate tobacco products. The new tobacco product container-closure system does not contain (b) (4) that may be present in trace quantities in the predicate tobacco product. To address whether these ingredient changes may cause the new tobacco product to raise different questions of public health, the applicant measured the quantities of pH, oven volatiles, formaldehyde, acetaldehyde, crotonaldehyde, benzo[a]pyrene, cadmium, arsenic, NNN, NNK, nicotine, nitrate, nitrite, water activity, and nicotine dissolution. The new and predicate tobacco products had similar nicotine dissolution curves with difference factor (f_1) and similarity factor (f_2) equal to 7 and 55, respectively. This suggests that the nicotine release rates for the new and predicate tobacco products are similar, and therefore differences between the products such as the quantities of pH adjuster and binder ingredients do not cause the new tobacco product to raise different questions of public health. The only HPHC yield that is not analytically equivalent between the new and predicate tobacco products is the 9% decrease in the mean quantities of total nicotine. The applicant demonstrated that the differences 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.

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 Pritesh Darji on October 28, 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:

- Tobacco cut size (b) (4) - deferred to Chemistry
- Average tobacco particle size (\uparrow 23%) - deferred to Chemistry

For the new tobacco product, tobacco cut size decreases and average tobacco particle size increases. 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 differs 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 mean tobacco 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.

Dissolution rate and constituent release data were submitted, and the evaluation of dissolution rate/constituent release data provided by the applicant was deferred to chemistry.

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 29, 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)
- 3% decrease in the amount of (b) (4)
- 3% decrease in (b) (4)
- 143% and 11% increases in total aerobic microbial counts (TAMC) at the (b) (4) and (b) (4) storage time points, respectively, when assessed in TNO culture medium
- 33% and 3% increases in TAMC at the (b) (4) storage time points, respectively, when assessed in TSA SB culture medium

The new and predicate tobacco products differ in overall duration of (b) (4) and decreases in (b) (4) components and the preservative (b) (4) that could potentially affect microbial growth which, in turn, could affect the microbial stability of the new tobacco product during storage. The applicant adequately addressed this concern by providing stability testing data for the new and predicate tobacco products. The microbial count (TAMC) data of the new tobacco product showed increases (at (b) (4) [143%] and (b) (4) [11%] in TNO; and at (b) (4) [33%] and (b) (4) [3%] in TSA SB) during product storage 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 ($\leq 15\%$), NNK ($\leq 18\%$), and total TSNA ($\leq 14\%$) compared to the predicate tobacco product at all storage timepoints. Therefore, the differences between the new and predicate tobacco products and the increases in TAMC of the new tobacco product compared to the predicate tobacco product are not of concern and do not cause the new tobacco product to raise different questions of public health from a microbiology perspective.

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 Thomas Hill on October 31, 2019.

The toxicology review concludes that the new tobacco product has different characteristics related to product 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:

- Ingredients other than Tobacco
 - 25% increase in (b) (4) mg/g)
 - 25% increase in (b) (4) mg/g)
 - Addition of (b) (4) mg/g)
 - Addition of (b) (4) mg/g of (b) (4) (0.025%)
 - Reduction of 13 other additives

Some ingredient changes were identified in the new tobacco product as compared to the predicate tobacco product. The applicant submitted HPHC yields, which can be used to show that ingredient changes do not cause the new tobacco product to raise different questions of public health. All of the HPHC yields are equivalent or lower in the new tobacco product; therefore, none of the ingredient changes cause the new tobacco product to raise different questions of public health. In addition, none of these ingredient changes are of toxicological 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 toxicology perspective.

5. ENVIRONMENTAL DECISION

Environmental reviews were completed by Shannon Hanna on October 29, 2019, November 13, 2019, and January 16, 2020.

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on January 24, 2020. The FONSI was supported by an environmental assessment prepared by FDA on January 24, 2020.

6. CONCLUSION AND RECOMMENDATION

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

- Tobacco blend: 10% less (b) (4), 3% less (b) (4) (no change in (b) (4) composition), and 10% (b) (4) mg/g) less total tobacco
- Ingredients:
 - Addition of (b) (4) and (b) (4)
 - 25% more (b) (4)
 - 10% less (b) (4)

- (b) (4)
- 3% less (b) (4)
 - 9% less (b) (4)
 - Container-closure system: removal of (b) (4)
 - Tobacco cut size (b) (4)
 - Average tobacco particle size (↑23%)
 - Change in overall duration of (b) (4)
 - 3% decrease in the amount of (b) (4) mg/g)
 - 3% decrease in (b) (4)
 - 143% and 11% increases in TAMC at the (b) (4) storage time points when assessed in TNO culture medium
 - 33% and 3% increases in TAMC at the (b) (4) storage time points when assessed in TSA SB culture medium

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 has less total tobacco and lower amounts of individual tobacco types compared to the predicate tobacco product, which does not cause the new product to raise different questions of public health. The new tobacco product has changes in many flavor ingredients and binders, but also has the addition of (b) (4) to the new tobacco product compared to the predicate tobacco product. The new tobacco product container-closure system does not contain (b) (4), which may be present in trace quantities in the predicate tobacco product. In addition, there is a change in the tobacco cut size and average tobacco particle size, which may affect dissolution rate/constituent release. To address whether these differences in characteristics may cause the new tobacco product to raise different questions of public health, the applicant measured the quantities of pH, oven volatiles, formaldehyde, acetaldehyde, crotonaldehyde, benzo[a]pyrene, cadmium, arsenic, NNN, NNK, nicotine, nitrate, nitrite, water activity, and nicotine dissolution. The new and predicate tobacco products had similar nicotine dissolution curves with difference factor (f_1) and similarity factor (f_2) equal to 7 and 55, respectively. This suggests that the nicotine release rates for the new and predicate tobacco products are similar, and, therefore, these differences in characteristics do not cause the new tobacco product to raise different questions of public health. Because most HPHC yields are equivalent in the new tobacco product than in the predicate tobacco product, the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

The new and predicate tobacco products differ in overall duration of (b) (4). Compared to the predicate tobacco product, the new tobacco product has a decrease in the (b) (4) components and the presence of a preservative, (b) (4), that could potentially affect microbial growth, which in turn could affect the microbial stability of the new tobacco product during storage. The applicant adequately addressed this concern by providing stability testing data for the new and predicate tobacco products and the new tobacco product showed lower levels of NNN ($\leq 15\%$), NNK ($\leq 18\%$), and total TSNA ($\leq 14\%$) compared to the predicate tobacco product at all storage timepoints. 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 SE0015469 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 Rooster Long Cut Wintergreen, which is a grandfathered tobacco product under GF1200066. 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:

- Tobacco blend: 10 – 11% less (b) (4), 5% less (b) (4) removal of (b) (4) component, and 10% (33 mg/g) less total tobacco
- Ingredients: Addition of (b) (4) and (b) (4) binders, 25% more (b) (4) binders, 50% less (b) (4) less (b) (4), 10% less (b) (4), 9% more (b) (4), 10% less (b) (4), 5% more (b) (4), 3% more (b) (4), 8% less (b) (4) and (b) (4), 4% less (b) (4), and 9% less (b) (4)
- Tobacco cut size (b) (4)
- Average tobacco particle size (↑23%)
- Change in container-closure system (plastic can with metal lid in new tobacco product vs. plastic can with plastic lid in grandfathered tobacco product)
- Changes in composition of (b) (4) resulting in addition of (b) (4) mg/g (b) (4) and addition of a preservative, (b) (4)
- Change in duration of (b) (4)

The differences in container closure system and composition of (b) (4), 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 SE0015469 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in tobacco blend, ingredients, tobacco cut size, average tobacco particle size, and change in duration of (b) (4) between the new tobacco product in SE0015469 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 SE0015469 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 SE0015469, as identified on the cover page of this review.