FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0015523

SE0015523: Copenhagen Premium Pouches Wintergreen	
Package Type	Plastic Can with Metal Lid
Package Quantity	24.0 g
Portion Count	12 Portions
Portion Mass	2000 mg
Portion Length	31.4 mm
Portion Width	23.4 mm
Portion Thickness	2.56 mm
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	Portioned Moist Snuff
Recommendation	
Issue Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Digitally signed by Jeannie H. Jeong-im -S
Date: 2020.05.19 16:04:16 -04'00'

Jeannie Jeong-Im, 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: 2020.05.19 16:36:33 -04'00'

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

TABLE OF CONTENTS

1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco product:

SE0015523: Copenhagen Premium Pouches Wintergreen	
Product Name	Skoal Pouches Wintergreen
Package Type	Plastic Can with Metal Lid
Package Quantity	23.25 g
Portion Count	15 Portions
Portion Mass	1550 mg
Portion Length	40 mm
Portion Width	18 mm
Portion Thickness	6.07 mm
Tobacco Cut Size	(b)(4) CPI
Characterizing Flavor	Wintergreen
Additional Property	Fine Cut

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On October 2, 2019, FDA received the SE Report from Altria Client Services, LLC (ALCS) on behalf of U.S. Smokeless Tobacco Company LLC. (USSTC). On October 8, 2019, FDA issued an Acceptance letter to the applicant.

On December 18, 2019, FDA issued a Deficiency letter to the applicant. On February 26, 2020, FDA received the applicant's response to the Deficiency letter (SE0015731).

Product Name	SE Report	Amendment
Copenhagen Premium Pouches Wintergreen	SE0015523	SE0015731

1.3. SCOPE OF REVIEW

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

2. REGULATORY REVIEW

A regulatory review was completed by Ebony Griffin on October 8, 2019. The review concluded 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 as of February 15, 2007). The OCE review dated November 4, 2019, conclude 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.

OCE also completed a review to determine whether the new tobacco product is 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 OCE review dated April 30, 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 27, 2019 and April 13, 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:

- 29% (0.45 g) larger portion size: new (b) (4) g and predicate (b) (4) g
  - Container-closure system: removal of Gold R/C Enamel
  - 47% larger tobacco cut size
- Tobacco blend:
  - 26% more (b) (4), and (b) (4) tobaccos and (b) (4) tobacco, and 26% (b) (4) mg/portion) more total tobacco
- Ingredients to tobacco:
  - 1080% (b) (4) mg/portion) more (b) (4); 164% (b) (4) mg/portion) more (b) (4); 57% more (b) (4) 12% more of (b) (4) mg/portion or less; and 20% more (b) (4).
- Pouch material design and composition differences
- Analytically non-equivalent HPHCs:
  - 18% less NNK, 7% more total nicotine, 23% more free nicotine, 41% more arsenic, 32% more acetaldehyde, and 32% less formaldehyde

The new tobacco product is 29% (0.45 mg/portion) larger than the predicate tobacco product, but the portion count decreased by 3 (from 15 to 12). The package size is 0.75 g/can larger between the new (24.00 g) and predicate tobacco products (23.25 g). The new tobacco product has 3% less total tobacco (mg/g), differences in many flavor ingredients, and different pouch

materials compared to the predicate tobacco product. For example, the new tobacco product has 79% ([redacted] mg/g) more [redacted] flavors than the predicate tobacco product. Differences in ingredients in tobacco were deferred to the toxicology reviewer. The new tobacco product container-closer system does not contain gold R/C enamel that may be present in trace quantities in the predicate tobacco product. The new tobacco product pouch material is mostly (b) (4), but the predicate tobacco product pouch material is mostly (b) (4), (b) (4), and polyethylene / polypropylene. The applicant measured HPHC quantities and nicotine dissolution extracted from the intact finished tobacco products. The applicant measured pH, oven volatiles, formaldehyde, acetaldehyde, crotonaldehyde, benzo[a]pyrene, cadmium, arsenic, NNN, NNK, nicotine, nitrate, nitrite, water activity, and nicotine dissolution. Comparing the new and predicate tobacco products, some HPHC results are not analytically equivalent: 18% less NNK, 7% more total nicotine, 23% more free nicotine, 41% more arsenic, 32% more acetaldehyde, and 32% less formaldehyde. These HPHC results were deferred to the toxicology reviewer. The new and predicate tobacco products had similar nicotine dissolution curves with a difference factor (f1) and a similarity factor (f2) equal to 8 and 58, respectively, suggesting that the nicotine release rates for the new and predicate tobacco products are similar. 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 Drew Katherine on November 24, 2019.

The engineering review concludes that the new tobacco product have 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:

- Difference in tobacco particle size distribution
- 29% increase in portion mass
- 22% decrease in portion length
- 30% increase in portion width
- 21% increase in pouch material basis weight
- Difference in pouch material air permeability
- 39% increase in pouch material thickness

The tobacco cutting processes and cut sizes were different between the new and predicate tobacco products. The new tobacco product was cut [redacted] while the predicate tobacco product was cut and [redacted], passed through a [redacted]. The (b) (4) (b) (4) test data showed a difference in particle size distribution. The difference in particle size may affect nicotine release rate. As such, the difference in particle size distribution is deferred to chemistry for the evaluation of nicotine release rates from the new and predicate products. (b) (4) (b) (4) . Also, the new and predicate tobacco products use different pouch materials. (b) (4) These differences are expected to affect nicotine release rates and have been

deferred to chemistry for the evaluation of nicotine release rates and the yields of nicotine as well as TSNAs. The new and predicate tobacco product air permeability target specifications and range limits were determined and tested by different test methods. Therefore, they are not directly comparable. It is not clear what the percentage difference in air permeability is between the new and predicate products. A difference in air permeability are expected to affect nicotine release rates. As such, the evaluation of nicotine release rates is deferred to chemistry. Therefore, the differences in characteristics between the new and 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 David L. Craft on November 27, 2019, and Aimee L. Cunningham on April 14, 2020.

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:

- Addition of [redacted] mg/g) in [redacted]
- Addition of [redacted] mg/g)
- Substitution of GRAS [redacted] mg/g) to replace an identical quantity of non-GRAS [redacted] in the [redacted]
- 2% decrease on target amount of [redacted]
- [redacted] duration of [redacted] days vs. [redacted] days

Water activity of the new tobacco product is 4-6% lower when compared to the predicate tobacco product during storage, with < 1% change in aw for both products over the storage period. A decrease in a_w may correlate with the TAMC data; TAMC was decreased ≥ 70% in the new tobacco product regardless of media type used in testing when compared to the predicate tobacco product at the beginning, middle, and end of storage. Increased TAMC (10%) of the new tobacco product on [redacted] compared to a 14% decrease in the predicate tobacco product over the storage period was mitigated by nitrate and nitrite levels which suggested that the increased bacterial load in the new tobacco product over storage was not due to an increase in nitrate-reducing bacteria. Nitrate levels were shown to be 32-33% lower during storage in the new tobacco product, and nitrite was below the limit of detection at all time points tested. To this end, levels of NNN, NNK, and total TSNAs of the new tobacco product were lower compared to the predicate tobacco product during storage (37-39% for NNN, 40-44% for NNK, and 39-41% for total TSNA levels). Taken together, this data suggests that the changes to the [redacted] and [redacted] duration in the new tobacco product do not affect stability of the new tobacco product, as changes to each stability parameter tested were of no concern. Therefore, compared to the predicate tobacco product, the new tobacco product does not raise different questions of public health from a microbiology perspective.

4.4. TOXICOLOGY

Toxicology reviews were completed by Mary Irwin on November 27, 2019 and April 13, 2020.

The final 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:

- Change of pouch material from (b) (4) to (b) (4) Pouch.
- Additions of [redacted]
- Increases in [redacted]
- Decreases in NNK (-18%) and formaldehyde (-32%) that offset increases in arsenic (41%) and acetaldehyde (32%) on a mass/portion basis

Daily exposure to HPHCs is not increased due to the addition of [redacted] exposure is lower than concern levels for thyroidal effects, with no other toxicological concerns. There is a change in pouch material in the new tobacco product relative to the predicate tobacco product. While not made to their specifications, the applicant provided the ingredients for the new material. These ingredients do not cause any toxicological concerns at this time. The increases in [redacted] remain below established oral toxicity levels, and therefore do not cause the new product to raise different questions of public health. The addition of [redacted] are without known oral toxicities. Therefore, these ingredients do not cause the new product to raise different questions of public health. There is increased exposure to [redacted] and consequently increased potential exposure to the cardiovascular toxicant glycyrrhizic acid. However, the potential daily exposure levels of glycyrrhizic acid due to heavy use (1 tin per day) of the new tobacco product remains below established oral exposure toxicity levels. Thus, the increase in [redacted] does not cause the new product to raise different questions of public health. Increases in arsenic (41%) and acetaldehyde (32%) may be offset by decreases in NNK (-18%) and formaldehyde (- 32%) on a mass/portion basis. Estimated daily exposure formaldehyde (-47%), NNN (-31%), NNK (-36%), cadmium (-12%), and benzo[a]pyrene (-9%) are decreased, offsetting increases of arsenic (11%) and acetaldehyde (3%) on a per daily exposure basis. Therefore, the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a toxicology perspective.

5. ENVIRONMENTAL DECISION

Environmental reviews were completed by Thomas Creaven on November 19, 2019 and March 25, 2020.

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on April 17, 2020. The FONSI was supported by an environmental assessment prepared by FDA on April 17, 2020.

6. CONCLUSION AND RECOMMENDATION

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

- 29% (0.45 g) larger portion size: new 2.000 g and predicate 1.5500 g
- Container-closure system: removal of Gold R/C Enamel
- 47% larger tobacco cut size (Difference in tobacco particle size distribution)
- 29% increase in portion mass
- 22% decrease in portion length
- 30% increase in portion width
- 21% increase in pouch material basis weight
- Difference in pouch material air permeability
- 39% increase in pouch material thickness
- Change of pouch material from (b) (4) to (b) (4) (b) (4) Pouch
- (b) (4)
- Tobacco blend:
  - 26% more (b) (4), and (b) (4) tobaccos and (b) (4) tobacco, and 26% ((b) (4) mg/portion) more total tobacco
  - Addition of (b) (4)
- Ingredients to tobacco:
  - 1080% ((b) (4) mg/portion) more (b) (4); 164% ((b) (4) mg/portion) more (b) (4); 57% more (b) (4); 12% more of (b) (4) ortion or less; and 20% more (b) (4).
  - Addition of (b) (4) GRAS (b) (4) mg/g)
  - Removal of non-GRAS (b) (4) mg/g)
- Analytically non-equivalent HPHCs:
  - 18% less NNK, 7% more total nicotine, 23% more free nicotine, 41% more arsenic, 32% more acetaldehyde, and 32% less formaldehyde

The pouch size increased by 29%, and, therefore, several ingredients added to the tobacco have increased or have been added. All these ingredients do not cause any toxicological concerns at this time, because they remain below established oral toxicity levels or are without known oral toxicities. There is a change in pouch material in the new tobacco product relative to the predicate tobacco product. While not made to their specifications, the applicant provided the ingredients for the new material. There are no known toxicities associated with oral exposure to the added ingredients at the levels present in the new tobacco product at this time. The applicant measured pH, oven volatiles, formaldehyde, acetaldehyde, crotonaldehyde, benzo[a]pyrene, cadmium, arsenic, NNN, NNK, nicotine, nitrate, nitrite, water activity, and nicotine dissolution. Comparing the HPHCs between the new and predicate tobacco products, some HPHC results are not analytically equivalent: 18% less NNK, 7% more total nicotine, 23% more free nicotine, 41% more arsenic, 32%

more acetaldehyde, and 32% less formaldehyde. Increases in arsenic and acetaldehyde may be offset by decreases in NNK and formaldehyde. Also, estimated daily exposure decreases for formaldehyde (47%), NNN (31%), NNK (36%), cadmium (12%), and benzo[a]pyrene (9%) offsets the increases of arsenic (11%) and acetaldehyde (3%) on a per daily exposure basis. The new and predicate tobacco products had similar nicotine dissolution curves with a difference factor (f1) and a similarity factor (f2) equal to 8 and 58, respectively, suggesting that the nicotine release rates for the new and predicate tobacco products are similar. Therefore, the differences in characteristics between the new and predicate product does not cause the new tobacco product to raise different questions of public health.

The predicate tobacco product meets statutory requirements because it was determined that it 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 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 SE order letters be issued.

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

SE order letters should be issued for the new tobacco product in SE0015523, as identified on the cover page of this review.