FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0015250

SE0015250: Grizzly Premium Natural Fine Cut	
Package Type	Plastic Can with Metal Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) Cuts per Inch (CPI)
Characterizing Flavor	None
Attributes of SE Report	
Applicant	American Snuff Company LLC
Report Type	Regular
Product Category	Smokeless Tobacco Product
Product Sub-Category	Loose Moist Snuff
Recommendation	
Issue Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Digitally signed by Todd L. Cecil -S
Date: 2019.11.22 13:21:07 -05'00'

For Gloria Kulesa
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: 2019.11.22 13:28:03 -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:

SE0015250: Grizzly Premium Natural Fine Cut	
Product Name	Grizzly Premium Natural Fine Cut
Package Type	Plastic Can and Lid
Package Quantity	34.02 grams
Tobacco Cut Size	(b) (4) CPI
Characterizing Flavor	None

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 May 30, 2019, FDA received one Substantial Equivalence (SE) report from RAI Services Company on behalf of American Snuff Tobacco Company, LLC. FDA issued an Acknowledgement letter to the applicant on June 6, 2019. On August 7, 2019, FDA issued a Deficiency letter. In response, FDA received amendment SE0015411 from the applicant on August 26, 2019.

Product Name	SE Report	Amendment
Grizzly Premium Natural Fine Cut	SE0015250	SE0015411

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 Shontelle Dixon on June 6, 2019. The 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 June 28, 2019, 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.

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) (see section 910(a)(2)(A)(i)(II) of the FD&C Act). The OCE reviews dated July 30, 2019 and November 1, 2019, conclude that the new tobacco product is in compliance with the FD&C Act.

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 Karina Zuck on July 19, 2019 and October 10, 2019[1].

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:

- NNN (↓48%)
- NNK (↓45%)
- Increase in free nicotine

The applicant submitted NNN, NNK, free nicotine and total nicotine measured in three batches of tobacco filler in the new and predicate tobacco products. There is a decrease in NNN and NNK do not raise different questions of public health from a chemistry perspective. There is significant variability in the calculated free nicotine between the three batches. Free nicotine is 16% lower in the new tobacco product compared to the predicate tobacco product in batch 1, but 24-28% higher in batch 2 and batch 3. A change in calculated free nicotine values suggest that the nicotine release rates may differ between the new and predicate tobacco products. In addition, the applicant stated that there was an increase in small cut size tobacco particles in the tobacco blend. A smaller tobacco particle size has a greater surface area, which may result in an increase in the release rate of nicotine. Changes in the nicotine release rate may result in changes in user behavior. The applicant provided a nicotine dissolution study which includes measurements of nicotine release rates and total nicotine content release in the new and predicate tobacco products. The dissolution profiles were compared and indicate that the dissolution profiles of the new and predicate tobacco products are equivalent. Therefore, the differences in the tobacco cut size and free nicotine do not cause the new tobacco product to raise different questions of public health from a chemistry perspective.

[1] An addendum review was completed on November 21, 2019, amending section 3.1 Key Differences of the October 10, 2019, review to reflect the resolved issues.

4.2. ENGINEERING

An engineering review was completed by Michael Morschauser on July 18, 2019.

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

- Decrease in tobacco moisture (3%)
- Decrease in tobacco cut size

The change in tobacco moisture is anticipated to be too small to affect the amount and rate of constituents released from the product and does not cause the new tobacco product to raise different questions of public health. The applicant stated that there was an increase in small cut size tobacco particles in the tobacco blend. Smaller particle size tobacco has a greater surface area, which may result in an increase in the release rate of nicotine. Changes in the nicotine release rate may result in changes in user behavior. The potential change in the nicotine release rate was deferred to chemistry for their evaluation. 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 Wen Lin on July 15, 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 container closure system (replacement of plastic lid with metal lid)
- 2% - 4% lower moisture content (OV%) at (b) (4) of product storage
- 3% - 64% higher TAMC at (b) (4) of product storage and 41% lower TAMC at (b) (4) storage
- Increase (340 vs 877%) in TAMC over the storage time of (b) (4)
- 32% - 94% lower nitrite at (b) (4) of product storage
- Increase (2561 vs 4281%) in nitrite over the storage time of (b) (4)
- 46% - 51% lower NNN, at (b) (4) of product storage
- 45% - 52% lower NNK, at (b) (4) of product storage
- 52% - 55% lower total TSNA, at (b) (4) of product storage

The new and predicate tobacco products differ in the container closure system, which could potentially affect the OV% and, in turn, impact microbial growth. This could potentially affect the microbial stability of the new tobacco product since microbial-mediated nitrite accumulation plays a key role in the TSNA levels of the finished tobacco product during storage. The applicant provided product stability data measured over the complete storage time of the new and

predicate tobacco products. The OV% of the new tobacco product is lower (2 – 4%) than the predicate tobacco product throughout storage. However, except for the end of product storage, the TAMC of the new tobacco product was higher (3 – 64%) than the predicate tobacco product at each measured time point. These increases in TAMC are not of concern because the new tobacco product showed lower levels of nitrite (32 – 94%), NNN (46 – 51%), NNK (45 – 52%) and total TSNAs (52 – 55%) compared to the predicate tobacco product at each measured time point. However, over the storage time of (b) (4) , the new tobacco product showed increases in nitrite and TAMC. Although the new tobacco product showed lower increases in nitrite (2561 vs 4281%, respectively) and TAMC (340 vs 877%, respectively) compared to the predicate tobacco product, they could still be of concern if resulted in increases in TSNAs during storage. However, this concern is adequately addressed based on the 1% increase in TSNAs over the (b) (4) storage time of the new and predicate tobacco products. In conclusion, the change in container closure system of the new tobacco product compared to the predicate tobacco product does 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.

5. ENVIRONMENTAL DECISION

Environmental reviews were completed by William Brenner on July 10, 2019[2].

A finding of no significant impact (FONSI) was signed by Kimberly Benson on July 12, 2019. The FONSI was supported by an environmental assessment prepared by FDA on July 12, 2019.

6. CONCLUSION AND RECOMMENDATION

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

- NNN (↓48%)
- NNK (↓45%)
- Decrease in tobacco moisture
- Increase in free nicotine
- Decrease in tobacco cut size
- Change in container closure system (replacement of plastic lid with metal lid)
- Lower moisture content (OV%) at (b) (4) of product storage
- Higher TAMC at (b) (4) of product storage and 41% lower TAMC at (b) (4) storage
- Increase (340 vs 877%) in TAMC over the storage time of (b) (4) s
- Lower nitrite at (b) (4) months of product storage
- Increase (2561 vs 4281%) in nitrite over the storage time of (b) (4)
- Lower NNN, at (b) (4) of product storage

[2] A second environmental review was completed on September 24, 2019, following the applicant's response to the August 7, 2019 Deficiency letter. The review concludes the information in the amendment does not affect the analysis and conclusions in the environmental assessment prepared by FDA on July 12, 2019.

- Lower NNK, at (b) (4) of product storage
- Lower total TSNA, at (b) (4) of product storage

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. The applicant provided NNN, NNK, Nicotine, moisture, and pH measurements for the new and predicate tobacco products. The stated NNN and NNK content in the new tobacco product is lower than the content in the predicate tobacco product. A decrease in the NNN and NNK do not cause the new tobacco product to raise different questions of public health. The new and predicate tobacco products have identical machine settings and design specifications, except for a 3% decrease in the product moisture. The change in tobacco moisture is anticipated to be too small to affect the amount and rate of constituents released from the product. Therefore, the change in moisture does not cause the new tobacco product to raise different questions of public health. In addition, the applicant identified an increase in the smaller tobacco particle size distribution obtained from the tobacco cutting operation. An increase in the smaller tobacco particle size may increase the amount and rate of nicotine released from the tobacco product. The applicant provided dissolution results that indicated that the nicotine release rates of the new and predicate tobacco products are equivalent. The applicant provided measured levels for free nicotine and total nicotine which demonstrated significant variability in the calculated free nicotine. A change in the calculated free nicotine values suggest that the nicotine release rates may differ between the new and predicate tobacco products. As indicated above, the applicant provided dissolution results that indicated that the nicotine release rates of the new and predicate tobacco products are equivalent. Therefore, the differences in free nicotine levels of the new and predicate tobacco products do not raise different questions of public health. The containers hold the same overall quantity of tobacco, are made of plastic, but differ in the type of lid used (a metal lid for the new product and a plastic lid for the predicate product) which may result in changes to moisture and possibly impact microbial growth. The stability of the new tobacco product was evaluated through changes in the TSNA levels of the finished tobacco product during storage. These HPHCs decreased over time, which indicated that the change in moisture did not result in an increase in microbial growth. Therefore, the change in the container closure system 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.

The predicate tobacco product meets statutory requirements because it was determined that it is a grandfathered tobacco 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, the scientific review concludes 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 SE0015250, as identified on the cover page of this review.