FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0015282

SE0015282: Marlboro 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Characterizing Flavor	None
Length	98 mm
Diameter	7.89 mm
Ventilation	15%
Attributes of SE Report	
Applicant	Philip Morris USA Inc.
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Digitally signed by Charles Feng -S
Date: 2020.04.21 13:21:09 -04'00'

Charles Feng, 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: 2020.04.21 13:36:48 -04'00'

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:

SE0015282: Marlboro 100's Soft Pack	
Product Name	Marlboro 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 Cigarettes
Characterizing Flavor	None
Length	98 mm
Diameter	7.89 mm
Ventilation	15%

The predicate tobacco product is a combusted filtered cigarette manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On June 28, 2019, FDA received one SE Report from Altria Client Services LLC, on behalf of Philip Morris USA Inc. FDA issued an Acknowledgment letter to the applicant on July 8, 2019. On August 30, 2019, FDA issued a Deficiency letter to the applicant. On January 28, 2020, FDA received an amendment containing a response to the Deficiency letter (SE0015659).

Product Name	SE Report	Amendments
Marlboro 100's Soft Pack	SE0015282	SE0015659

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 Samuel Motto on July 8, 2019.

The review concludes that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The predicate tobacco product in SE0015282 was determined to be substantially equivalent by FDA under SE0014711. 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 April 3, 2020, concludes 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 Samantha Reilly on August 15, 2019, and Scott Wasdo on March 17, 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 Filler Ingredients:

- Removal of (b) (4) mg/cigarette)
- Decrease in (b) (4) (↓ 48%, (b) (4) mg/cigarette)
- Addition of (b) (4) mg/cigarette)
- Increase in (b) (4) (↑1,043%, (b) (4) mg/cigarette)

Cigarette Paper Ingredients:

- Decrease in (b) (4) (↓8%, (b) (4) /cigarette)
- Decrease in (b) (4) (↓11%, (b) (4) mg/cigarette)
- Removal of (b) (4) mg/cigarette)
- Decrease in (b) (4) (↓14%, (b) (4) mg/cigarette)
- Removal of (b) (4) mg/cigarette)
- Increase in (b) (4) (↑25%, (b) (4) mg/cigarette)
- Increase in (b) (4) (↑231%, (b) (4) mg/cigarette)
- Increase in (b) (4) (↑65%, (b) (4) mg/cigarette)
- Addition of (b) (4) mg/cigarette)

Tipping Adhesive:

- Addition of (b) (4) mg/cigarette)

The applicant provided a certification statement that, except for the components mentioned above, the materials, ingredients, design features, heating source, or any other feature of the new tobacco product are identical to those of the predicate tobacco product.

Significant product composition issues are primarily limited to one tipping adhesive ingredient difference, one complex flavor ingredient changing composition, and a difference in cigarette paper weight due to differences in several individual ingredient quantities in the cigarette paper between the new and predicate product. The difference in tipping adhesive and the

complex flavor are not expected to affect smoke chemistry because they are either not expected to be combusted or too small to cause measurable changes in HPHC yields. However, the differences in cigarette paper ingredients could affect smoke yields of tar, nicotine, and carbon monoxide (TNCO), acetaldehyde, acrolein, benzene, benzo[a]pyrene (B[a]P), crotonaldehyde and formaldehyde. The engineering review also identified differences in cigarette paper band porosity and cigarette paper band width that may affect TNCO and B[a]P yields and deferred the evaluation of such to chemistry.

The applicant submitted TNCO, acetaldehyde, acrolein, benzene, B[a]P, crotonaldehyde, formaldehyde, and toluene smoke yields measured under the ISO and CI smoking regimens. All the HPHC smoke yields in the new tobacco product were analytically equivalent to values provided for the predicate tobacco product. The applicant also provided information for the methods including standard test protocols, validation reports and data for reference products analyzed at the same time as the new and predicate tobacco product. This information was sufficient to verify the methods used to measure the TNCO and other HPHC yields reported in SE0015282. Since the smoke yields of TNCO and the other tested HPHCs are analytically equivalent in the new and predicate tobacco product, the ingredient differences between the new and predicate tobacco product identified in SE0015282 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 product 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 Robert Meyer on August 15, 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:

- 125% higher band porosity
- 8% lower band width

With exception of the cigarette paper, the new and predicate tobacco products have same design parameters. There are differences in cigarette paper band porosity and cigarette paper band width, which may impact TNCO and B[a]P yields. The evaluation of the yields of TNCO and B[a]P is deferred to chemistry.

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

4.3. TOXICOLOGY

Toxicology reviews were completed by Prabha Kc on August 15, 2019[1], and March 17, 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:

- Addition of [redacted] mg/cigarette)
- Increase in [redacted] (↑1,043%, [redacted] mg/cigarette)
- Addition of [redacted] mg/cigarette)
- Increase in [redacted] (estimated ↑4 %, [redacted] mg/cig)
- Decrease in [redacted] (↓11%, [redacted] mg/cigarette)
- Decrease in [redacted] (↓14%, [redacted] mg/cigarette)
- Increase in [redacted] (↑25%, [redacted] mg/cigarette)
- Increase in [redacted] (↑231%, [redacted] mg/cigarette)
- Addition of [redacted] mg/cigarette)

Although there were increases or addition of [redacted], these changes do not have toxicological concerns because 1) the estimated daily intake of these ingredients are lower than the established or estimated toxicological values, and 2) the potential HPHCs yields were analytically equivalent. The decreases in [redacted] and [redacted] may affect burn rate, however, these changes do not raise concerns because of the analytically equivalent HPHC yields. The addition of [redacted] in the tipping paper is not expected to be burned, volatilized or to be a potential source of HPHCs for inhalation exposure. Therefore, this change is not of toxicological concern.

In the cigarette paper, cocoa extract was increased (↑1043%; [redacted] mg/cig) in the new tobacco product. However, the applicant clarified that the amount of [redacted] disclosed in SE0015282 Report dated June 28, 2019, contained [redacted] in the new tobacco product, whereas the predicate tobacco product reflected only the [redacted]. The quantity of [redacted] is actually less in the new tobacco product [redacted] mg/cig) compared to the predicate tobacco product [redacted] mg/cig), therefor, there are no toxicological concerns from [redacted] in the new tobacco product.

The toxicology review conservatively estimated that there could be a small increase in [redacted] (↑4%; [redacted] mg/cig), using the assumption that the amount of this ingredient in the [redacted] to be 100%. Pyrolysis of [redacted] can form HPHCs such as acetaldehyde. Considering the acetaldehyde yield is analytically equivalent between the new and predicate tobacco product, even with this conservative overestimation, the change in [redacted] does not cause the new tobacco product to raise different questions of public health from a toxicological perspective. Note that the chemistry review found a small decrease in [redacted] by 48% ([redacted] mg/cigarette), using the quantities (percentage values) provided by the applicant. I, as TPL, determined that the toxicology's evaluation of (b) (4) based on a

[1] An addendum review was completed on August 29, 2019, to correct a typographical error found in the deficiency language in the 1stToxicology review

conservative estimation does not cause the new product to raise different questions of public health with regard to the change in [redacted]. And for the purpose of this TPL review, I determined that the chemistry's finding should be reported.

[redacted] was added [redacted] mg/cig) to the cigarette paper in the new tobacco product. From a toxicological perspective, potential pyrolysis products from [redacted] of toxicological concern included [redacted]. The applicant stated that the TNCO and select HPHC yields (specifically formaldehyde and acetaldehyde) are comparable between the new product and predicate tobacco product, and as such, addition of [redacted] to cigarette paper does not cause a new product to raise different questions of public health. However, the toxicological concerns that arise from a potential pyrolysis product of [redacted] cannot be offset by the HPHCs that are considered analytically equivalent between the new and predicate tobacco product. Based on the available literature, considering 0.1% of [redacted] undergoes pyrolysis, the toxicology review assessed the daily exposures of [redacted] and [redacted] l from pyrolysis of [redacted] in the new tobacco product. Using these considerations, the intake amounts of [redacted] and [redacted] are 8 and 30-folds, respectively, lower than the estimated daily exposures of [redacted] from the new tobacco product. Thus, there are no concerns from the toxicological perspective for these constituents.

Therefore, the differences in characteristics between the new and predicate tobacco product 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 August 13, 2019 and March 10, 2020.

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

6. CONCLUSION AND RECOMMENDATION

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

Tobacco Filler Ingredients:

- Removal of [redacted] mg/cigarette)
- Decrease in [redacted] (↓ 48%, [redacted] mg/cigarette)
- Addition of [redacted] mg/cigarette)
- Increase in [redacted] (↑1,043%, [redacted] mg/cigarette)

Cigarette Paper Ingredients and design parameters:

- Decrease in [redacted] (↓8%, [redacted] mg/cigarette)
- Decrease in [redacted] (↓11%, [redacted] mg/cigarette)
- Removal of [redacted] mg/cigarette)
- Decrease in [redacted] (↓14%, [redacted] mg/cigarette)

- Removal of [redacted] mg/cigarette)
- Increase in [redacted] (↑25%, [redacted] mg/cigarette)
- Increase in [redacted] (↑231%, [redacted] mg/cigarette)
- Increase in [redacted] (↑65%, [redacted] mg/cigarette)
- Addition of [redacted] mg/cigarette)
- 125% higher band porosity
- 8% lower band width

Tipping Adhesive:

- Addition of [redacted] mg/cigarette)

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. Significant product composition issues are primarily limited to one tipping adhesive ingredient difference, one complex flavor ingredient changing composition, and a difference in cigarette paper weight due to differences in several individual ingredient quantities in the cigarette paper between the new and predicate product. The difference in tipping adhesive and the complex flavor are not expected to affect smoke chemistry because they are either not expected to be combusted or too small to cause measurable changes in HPHC yields. However, the differences in cigarette paper ingredients could affect smoke yields of tar, nicotine, and carbon monoxide (TNCO), acetaldehyde, acrolein, benzene, B[a]P, crotonaldehyde and formaldehyde. The engineering review also identified differences in cigarette paper band porosity and cigarette paper band width that may affect TNCO and B[a]P yields. The applicant submitted TNCO, acetaldehyde, acrolein, benzene, B[a]P, crotonaldehyde, formaldehyde, and toluene smoke yields measured under the ISO and CI smoking regimens. All the HPHC smoke yields in the new tobacco product were analytically equivalent to values provided for the predicate tobacco product. Addition of [redacted] may result in increases in [redacted] However, based on the available literature, the toxicology review calculated that the intake amounts of [redacted] are 8 and 30-folds, respectively, lower than the estimated daily exposures of [redacted] from the new tobacco product. Therefore, the differences in characteristics between the new and predicate tobacco product do not cause the new tobacco product to raise different questions of public health.

The predicate tobacco product was previously determined to be substantially equivalent by FDA under SE0014711.

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 SE0015282 was previously determined to be substantially equivalent by FDA under SE0014711. Comparison of the new tobacco product to the grandfathered tobacco product (Marlboro 100's Box in SE0014711) reveals that the new tobacco product has the following differences in characteristics from Marlboro 100's Box, the grandfathered tobacco product:

- Decrease in [redacted]

- Decrease in (b) (4)
- Increase in (b) (4)
- Decrease in (b) (4)
- Addition of (b) (4)
- Decrease in (b) (4)
- Increase in (b) (4)
- Increase in (b) (4)
- Addition of (b) (4)
- Increase in (b) (4)
- Addition of (b) (4)
- Addition of (b) (4)
- Increase in filter total denier
- Addition of (b) (4) in tipping adhesive

The differences in characteristics listed above, other than the differences in tipping adhesive are the same as or similar to the differences in characteristics identified for the new and grandfathered tobacco product in SE0014711. Therefore, these differences do not cause the new tobacco product in SE0015282 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in tipping adhesive between the new tobacco product in SE0015282 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 SE0015282 to the predicate or grandfathered tobacco product, 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 product 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 letters 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 SE0015282, as identified on the cover page of this review.