FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review:

SE0014795

SE0014795: Marlboro Midnight Menthol Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	79 mm
Diameter	7.89 mm
Ventilation	12%
Characterizing Flavor	Menthol
Common Attributes of SE Reports	
Applicant	Philip Morris USA Inc.
Report Type	Regular
Product Category	Cigarettes
Product Sub-Category	Combusted, Filtered
Recommendation	
Issue a Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Jeannie H. Jeong-im -S 2019.02.04 14:21:05 -05'00'

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: 2019.02.04 18:00:03 -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:

SE0014795: Marlboro Midnight Menthol Box	
Product Name	Marlboro Menthol Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter	7.89 mm
Ventilation	21%
Characterizing Flavor	Menthol

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On June 27, 2018, FDA received one Substantial Equivalence (SE) Report (SE0014795) from Altria Client Services LLC (ALCS) on behalf of Philip Morris USA Inc. (PMUSA). FDA issued an Acknowledgement letter to the applicant on July 13, 2018. FDA issued a correction letter on July 25, 2018, to correct the company name listed in the Acknowledgment letter. FDA issued an Advice/Information (A/I) Request letter for SE0014795 on September 7, 2018. On November 6, 2018, FDA received the applicant's response to the A/I Request letter (SE0014929).

Product Name	SE Report	Amendments
Marlboro Midnight Menthol Box	SE0014795	SE0014929

1.3. SCOPE OF REVIEW

This review captures all regulatory, compliance, and scientific reviews completed for these SE Reports.

2. REGULATORY REVIEW

A regulatory review was completed by Ryan Nguy on July 13, 2018, for the SE Report.

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 as of February 15, 2007). The OCE review dated August 3, 2018 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), as required by section 905(j)(1)(A)(i) of the FD&C Act. The OCE review dated February 1, 2019 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 Stephanie Daniels on August 21, 2018 and on January 7, 2019.

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 does not cause the new tobacco product to raise different questions of public health. The review identified the following differences:

- (b) (4), (b) (4), (b) (4) were present in the new product and not present in the predicate product.
- (b) (4) levels in new tobacco product were 17% higher than the predicate product.
- Several HPHCs in mainstream smoke yields of the new tobacco product were not analytically equivalent to the respective quantities in the predicate tobacco product under ISO and CI machine-smoking regimens. The following HPHCs were higher for the new tobacco product:

  o ISO Smoking Regimen
  - NNN (18%)
  - Ammonia (69%)

  o Cl Smoking Regimen
  - Ammonia (39%)

The total amount of (b) (4), (b) (4), (b) (4), (b) and (b tobacco were lower in the new tobacco product compared to the predicate tobacco product and (b), (b), and (b) were present in the new tobacco product. The differences of tobacco composition were evaluated by comparing the mainstream smoke HPHCs yields of the new tobacco product to the corresponding predicate tobacco product. The HPHC quantitative testing information was sufficient to determine that the HPHC data is reliable. This review determined that several HPHC quantities measured under ISO and CI smoking regimens were higher in the new tobacco product compared to the predicate tobacco product. An equivalence test determined most of HPHCs data submitted by the

applicant were statistically equivalent, which indicates that the higher quantities of HPHCs between the new and predicate tobacco products do not cause the new product to raise different questions of public health. However, some HPHC yields were not analytically equivalent. NNN and ammonia mainstream smoke yields were 18% and 69% higher, respectively, under the ISO smoking regimen; ammonia was 39% higher under Cl smoking regimen in the new tobacco product compared to the predicate tobacco product. The increased HPHC smoke yields in the new tobacco product and their toxicological effects were deferred to Toxicology. Therefore, based on the entirety of the chemistry information provided, the applicant has provided sufficient information demonstrating the differences between the new and predicate tobacco products do not cause the new product to raise different questions of public health.

4.2. ENGINEERING

An engineering review was completed by Robert Meyer on August 15, 2018.

The engineering review concludes that the new tobacco product has different characteristics related to product engineering compared to the corresponding 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:

- Puff count decreased by 10% in the new product compared to the predicate product.
- Base paper porosity increased by 82% in the new product compared to the predicate product.
- Band width decreased by 17% in the new product compared to the predicate product.
- Total denier increased by6% in the new product compared to the predicate product.
- Filter length decreased by10% in the new product compared to the predicate product.
- Filter ventilation decreased by43% in the new product compared to the predicate product.

Puff Count: 10% decrease: The new product's puff count is 10% less in comparison to the predicate product's puff count when evaluated using ISO testing methods. The new product puff count is the same as the predicate product's puff count (9.8 puffs) when evaluated using Canadian Intense smoke testing regimens. A decrease in puff count correlates to decreases in smoke constituents if the smoking ingredients are equivalent, and thus the puff count differences do not raise different questions concerning public health.

Base Paper Porosity: 82% increase: The new product cigarette base paper porosity target specification is 82% more porous in comparison to the predicate product's cigarette base paper porosity target specification. An increase in paper porosity allows surrounding air to more easily enter the smoke stream during inhalation, which causes the smoke constituent quantity per inhalation to decrease. From an engineering perspective, the increased cigarette base paper porosity does not cause the new product to raise different questions concerning public health.

Band Width: 17% decrease: The new product cigarette paper band width is 17% thinner in comparison to the corresponding predicate product band width. The function of the band is to temporarily reduce surrounding air from contacting the burning coals, which also locally

prevents air from entering the smoke stream. By decreasing the band width, the new product's environmental air to smoke constituent ratio will improve in favor of public health. Thus, from an engineering perspective, the decrease in band width target specification does not cause the new product to raise different questions of public health.

Total Denier: 6% increase: The new product total denier target specification increased 6% in comparison to the predicate product total denier target specification. An increase in total denier will not increase smoke constituent yields. If the denier per filament is constant, and the total denier increases then the filters ability to trap smoke particles improves. Thus, this difference does not raise different questions of public health from an engineering perspective.

Filter Length: 10% decrease: The new product filter length is 10% shorter (2mm) in comparison to the filter length of the predicate product. A difference in filter length may affect filter efficiency and, in turn, smoke constituent yields. The effects of the differences in filters may be offset by the increased paper porosity, yet this will be determined in the TNCO and HPHC evaluation. The applicant provided TNCO test values, and according to the chemist several differences in constituent measurements raise concerns. The TNCO and HPHC evaluation is deferred to chemistry.

Filter Ventilation: 43% decrease: The new product has 43% less filter ventilation in comparison to the filter ventilation of the predicate product. Less filter ventilation allows less environmental air to enter the smoke stream, which may expose the user to additional smoke constituents. The applicant reasons the decrease in filter ventilation by deferring to the HPHC and TNCO tests results that they provided. The chemistry reviewer confirmed that the TNCO values raise several concerns. The detailed evaluation of HPHC and TNCO test results is deferred to chemistry.

4.3. TOXICOLOGY

Toxicology reviews were completed by Steven Yee on August 17, 2018 and on January 7, 2019.

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

- There were multiple tobacco blend changes in the new product compared with the corresponding predicate product.
- Multiple ingredients were added or increased in the new product in comparison to the corresponding predicate product.
- Ammonia (ISO and CI) and NNN (ISO) increases in the new product compared to the predicate product

The applicant provided TNCO, NNN, NNK, B[a]P, acetaldehyde, acrolein, ammonia, benzene, 1,3-butadiene, formaldehyde, toluene, cresols (o-, m-, and p-), benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[f]furan, ethylene oxide, furan, methyl ethyl ketone, naphthalene, phenol, propionaldehyde, propylene oxide, styrene, and vinyl acetate under ISO and CI smoking regimens. All are within the expected variability of the methods, except for increases NNN (18%,

ISO) and ammonia (69%, ISO; 39%, CI). The applicant provided an abbreviated quantitative risk assessment (QRA) to support the claim that the increase in these HPHCs do not cause the new product to raise different questions of public health. The significant increase in ammonia and NNN in the new product were offset by significant decreases in formaldehyde and propylene oxide, as well as (potentially) other carcinogenic and non-carcinogenic HPHCs, which have similar or overlapping target organs and primary effects in the new product compared to the predicate product under both ISO and CI smoking regimens. Hence, the information provided to date supports a finding that the new product does not raise different questions of public health from a toxicology perspective.

5. ENVIRONMENTAL DECISION

Environmental reviews were completed by Dilip Venugopal on August 23, 2018 and on December 3, 2018. A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on February 1, 2019. The FONSI was supported by an environmental assessment prepared by FDA on February 1, 2019.

6. CONCLUSION AND RECOMMENDATION

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

- (b) (4), (b) (4), and (b) (4) were present in the new product and not present in the predicate product.
- (b) (4) levels in new tobacco product were 17% higher than the predicate product.
- Several HPHCs in mainstream smoke yields of the new tobacco product were not analytically equivalent to the respective quantities in the predicate tobacco product under ISO and CI machine-smoking regimens. The following HPHCs were higher for the new tobacco product:

  o ISO Smoking Regimen
  - NNN (18%)
  - Ammonia (69%)

  o CI Smoking Regimen
  - Ammonia (39%)
- Puff count decreased by 10% in the new product compared to the predicate product.
- Base paper porosity increased by 82% in the new product compared to the predicate product.
- Band width decreased by 17% in the new product compared to the predicate product.
- Total denier increased by6% in the new product compared to the predicate product.
- Filter length decreased by10% in the new product compared to the predicate product.
- Filter ventilation decreased by43% in the new product compared to the predicate product.

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. (b) (4) (mg/cig), (b) (4) (b)(5) Attorney-Client Privilege mg/cig),

and (b) (4) ((b)(5) Attorney-Client Privilege mg/cig) were present in the new product and not present in the predicate product. However, (b) (4) decreased by 76% ((b)(5) Attorney-Client Privilege mg/cig) and ((b)(5) Attorney-Client Privilege tobacco decreased by 16% ((b)(5) Attorney-Client Privilege mg/cig) in the new product compared with the predicate product. Also, there was a 3 – 7% decrease in the other tobaccos, which is a result of the 5% decrease (4 mm) in cigarette length and a 10% (2 mm) decrease in filter length. There was also a 10% decrease in puff count, 82% increase in base paper porosity, 17% decrease in band width, 6% increase in total denier, and 43% increase in filter ventilation. The applicant provided TNCO, NNN, NNK, B[a]P, as well as other HPHCs: acetaldehyde, acrolein, ammonia, benzene, 1,3-butadiene, formaldehyde, toluene, cresols (o-, m-, and p-), benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[f]furan, ethylene oxide, furan, methyl ethyl ketone, naphthalene, phenol, propionaldehyde, propylene oxide, styrene, and vinyl acetate under ISO and CI smoking regimens. All are within the expected variability of the methods, except for the following increases NNN (18%, ISO) and ammonia (69%, ISO; 39%, CI). The applicant provided an abbreviated quantitative risk assessment (QRA) to support the claim that the increase in these HPHCs do not cause the new product to raise different questions of public health. The significant increase in ammonia and NNN in the new product were offset by significant decreases in formaldehyde and propylene oxide, as well as (potentially) other carcinogenic and non-carcinogenic HPHCs, which have similar or overlapping target organs and primary effects in the new product compared to the predicate product under both ISO and CI smoking regimens. Hence, overall ingredient, design parameter, and HPHC changes in the new product in comparison to the predicate product are unlikely to cause the new product to raise different questions of public health. There is a 17% increase in (b) (4) in the new product compared to the predicate product. The applicant provided ISO and CI smoke data showing that (b) (4) actually decreases by 8 – 25% in the new product compared to the predicate product. The increase in (b) (4) in the new product does not raise different questions of public health. Therefore, the differences in characteristics between the new and predicate 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 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 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 SE0014795, as identified on the cover page of this review.