Technical Project Lead (TPL) Review: SE0015563 - SE0015564

SE0015563: Marlboro Special Select (Red Pack) Box	
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	84.0 millimeters (mm)
Diameter[1]	7.89 mm
Ventilation	20%
Characterizing Flavor	None
SE0015564: Marlboro Special Select (Gold Pack) Box	
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	84.0 mm
Diameter[1]	7.89 mm
Ventilation	23%
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	Philip Morris USA Inc.
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted, Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

[1] The applicant submitted the circumference, which allowed for a calculation of diameter.

Technical Project Lead (TPL):

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Date: 2020.05.28 09:01:24 -04'00'

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: 2020.05.28 09:08:04 -04'00'

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

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0015563: Marlboro Special Select (Red Pack) Box	
Product Name	Marlboro Special Select (Red Pack) Box
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	84.0 mm
Diameter[1]	7.89 mm
Ventilation	20%
Characterizing Flavor	None
SE0015564: Marlboro Special Select (Gold Pack) Box	
Product Name	Marlboro Lights Soft Pack
Package Type	Soft Pack
Package Quantity	20 Cigarettes
Length	84.0 mm
Diameter[1]	7.89 mm
Ventilation	23%
Characterizing Flavor	None

The predicate tobacco products are combusted, filtered cigarettes manufactured by the applicant.

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On November 8, 2019, FDA received two SE Reports from Altria Client Services LLC on behalf of Philip Morris USA Inc. On November 18, 2019, FDA issued an Acceptance letter to the applicant. On February 5, 2020, FDA issued a Deficiency letter to the applicant. On March 20, 2020, FDA received the response (SE0015779) to the Deficiency letter.

Product Name	SE Report	Amendments
Marlboro Special Select (Red Pack) Box	SE0015563	SE0015779
Marlboro Special Select (Gold Pack) Box	SE0015564	

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 Grace Kaiyuan on November 18, 2019.

The review concludes that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The predicate tobacco product in SE0015563 was determined to be substantially equivalent by FDA under SE0014850. 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 applicant established that the predicate tobacco product in SE0015564 is a grandfathered product (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007). The OCE review dated November 21, 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.

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the new tobacco products are in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act) (see section910(a)(2)(A)(i)(II) of the FD&C Act). The OCE review May 27, 2020, concludes that the new tobacco products are 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 January 16, 2020 and May 4, 2020.

The final chemistry review concludes that the new tobacco products have different characteristics related to product chemistry 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:

- Cigarette paper
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)

  - Deletion of (b) (4) mg/cigarette)
- Bands
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
- Tipping paper adhesive
  - Addition of (b) (4)

The applicant certified that the new tobacco products have identical design features, tobacco blends, ingredients added to tobacco filler, and structural material ingredients (excluding cigarette paper, including bands, and tipping adhesive) compared to the corresponding predicate tobacco products. Changes in the cigarette paper may affect harmful and potentially harmful constituents (HPHC) yields. The applicant provided HPHC data and the two one-sided t-test (TOST) evaluation demonstrate the HPHC differences between the new and corresponding predicate tobacco products were analytically equivalent under International Organization of Standardization (ISO) and Canadian Intense (CI) smoking regimens for both SE Reports.

Initially, the applicant did not provide sufficient information for some of the testing methods (e.g., limit of quantification (LOQ) for determining volatile organic compounds (VOCs)) and datasets for the reference tobacco product(s) for carbonyls, VOCs, tobacco specific nitrosamines (TSNAs), ammonia, and benzo[a]pyrene. However, the applicant subsequently demonstrated that the methods used to analyze the new and corresponding predicate tobacco products were accurate, precise, sensitive and fit for their intended purpose. Therefore, the methods do not cause the new tobacco products to raise different questions of public health from a chemistry perspective.

Therefore, the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health from a chemistry perspective.

4.2. ENGINEERING

An engineering review was completed by Nashaat Rasheed on January 30, 2020.

The engineering review did not identify any differences in characteristics between the new and corresponding predicate tobacco products that could cause the new tobacco products to raise different questions of public health from an engineering perspective. Therefore, the differences in characteristics between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health related to product engineering.

4.3. TOXICOLOGY

A toxicology review was completed by Theresa Thekkudan on January 6, 2020.

The toxicology review concludes that the new tobacco products have different characteristics related to toxicology 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:

- Cigarette paper: [redacted] (↑5.35%), [redacted] (↑90.5%), [redacted] (added), [redacted] (added), [redacted] (added), and [redacted] (added)
- Tipping adhesive: [redacted] (added)

For both SE Reports, the only ingredient changes in the burned portion of the new tobacco products, compared to their corresponding predicate tobacco products, are in the cigarette paper. These changes are increases in [redacted] and [redacted] and additions of [redacted] In addition, for both SE Reports, [redacted] in the predicate products is replaced by a lesser quantity of [redacted] in the new products.

The added or increased cigarette paper ingredients can pyrolyze to form the following HPHCs in mainstream smoke (MSS):

- [redacted] acetaldehyde and CO
- [redacted] acetaldehyde, acrolein, benzo[a]pyrene, benzene, CO, and formaldehyde
- [redacted] acetaldehyde, acrolein, 1,3-butadiene, benzene, CO, and formaldehyde
- [redacted] benzo[*a*]pyrene, and CO
- [redacted] acetaldehyde, and formaldehyde

For both the SE Reports, the applicant provided HPHC data for all the HPHCs listed above in MSS under ISO and CI regimens, and these HPHC levels are analytically equivalent between the new and corresponding predicate tobacco products by a TOST analysis.

Moreover, burn modifiers such as [redacted] and [redacted] are known to modify puff counts, and in both the SE Reports, the puff counts for the new tobacco products are lower than the corresponding predicate tobacco products. This will likely result in lower user exposure to HPHCs from the use of the new tobacco products compared to the predicate tobacco products.

In addition, [redacted] is added to the tipping adhesive. Tipping adhesive is not expected to be burned or be a potential source of thermal degradation leading to the generation of HPHCs. The smoker is not expected to have direct oral or dermal contact with any residual [redacted] in the tipping adhesive as the glue is bound at the tipping paper seam which is covered by the tipping paper. Therefore, in both SE Reports, the addition of [redacted] to the tipping adhesive of the new tobacco products is unlikely to cause the new tobacco products to raise different questions of public health from a toxicological perspective.

Therefore, the differences in characteristics between the new and corresponding 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 Rudaina Alrefai-Kirkpatrick on December 19, 2019 and April 28, 2020.

A finding of no significant impact (FONSI) was signed by Luis G. Valerio Jr., Ph.D. on April 29, 2020. The FONSI was supported by an environmental assessment prepared by FDA on April 29, 2020.

6. CONCLUSION AND RECOMMENDATION

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

- Cigarette paper
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Increase in [redacted] (↑5.35%)
  - Increase in [redacted] (↑90.5%)
- Bands
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
- Tipping paper adhesive
  - Addition of [redacted]

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 certified that the new tobacco products have identical design features, tobacco blends, ingredients added to tobacco filler, and structural material ingredients (excluding cigarette paper, including bands, and tipping adhesive) compared to the corresponding predicate tobacco products. Changes in the cigarette paper may affect HPHC yields. A TOST evaluation determined the HPHC differences between the new and corresponding predicate tobacco products were analytically equivalent under ISO and Cl smoking regimens for both SE Reports. Moreover, burn modifiers such as [redacted] and [redacted] are known to modify puff counts, and in both the SE Reports, the puff counts for the new tobacco products are lower than the corresponding predicate tobacco products. This will likely result in lower user exposure to HPHCs from the use of the new tobacco products compared to the predicate tobacco products. In addition, [redacted] is added to the tipping adhesive, which is not expected to be burned or be a potential source of thermal degradation leading to the generation of HPHCs. The smoker is not expected to have direct oral or dermal contact with any residual [redacted] in the tipping adhesive as the glue is bound at the tipping paper seam which is covered by the tipping paper. Therefore, in both SE Reports, the addition of [redacted] to the tipping adhesive of the new tobacco products does not cause the new tobacco products to raise different questions of public health. Therefore, the

differences in characteristics between the new and corresponding predicate product do not cause the new tobacco product to raise different questions of public health.

The predicate tobacco product in SE0015564 meets statutory requirements because it was determined that is a grandfathered (GF) product (i.e., was commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

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 SE0015563 was previously determined to be substantially equivalent by FDA under SE0014850. Comparison of the new tobacco product to the GF product (Marlboro Medium Soft Pack in SE0014850) reveals that the new tobacco product has the following differences in characteristics from Marlboro Medium Soft Pack, the GF tobacco product:

Differences between the new and GF tobacco products that are the same as the differences between the new and predicate tobacco products:

- Addition of cigarette paper ingredients
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette
- Bands
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette
- Tipping paper adhesive
  - Addition of (b) (4)

Differences between the new and GF tobacco products that are same as the differences between the predicate and GF tobacco products:

- Base Tipping paper

  - Decrease in [redacted] by 64% ([redacted] mg/cigarette)
  - Increase in [redacted] by 211% ([redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
- Brown ink
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
- Buff ink
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion [redacted] mg/cigarette)
- Extender 2
  - Addition of [redacted] mg/cigarette)
  - Addition of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)
  - Deletion of [redacted] mg/cigarette)

The differences in characteristics listed above in the base tipping paper, brown ink, buff ink, and extender 2 are the same differences in characteristics identified for the new and grandfathered tobacco products in SE0014850. Therefore, these differences do not cause the new tobacco product in SE0015563 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in the cigarette paper, including the bands, and in the tipping paper adhesive between the new tobacco product in SE0015563 and the grandfathered tobacco products do not cause the new tobacco products to raise different questions of public health. Therefore, whether comparing the new tobacco product in SE0015563 to the predicate or grandfathered tobacco products, the new tobacco product does not raise different questions of public health.

The new tobacco products are currently in compliance with the FD&C Act. In addition, all of the scientific reviews conclude that the differences between the new and corresponding predicate tobacco products are such that the new tobacco products do 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 these new tobacco products substantially equivalent and made a finding of no significant impact.

SE order letters should be issued for the new tobacco products in SE0015563 and SE0015564, as identified on the cover page of this review.