Technical Project Lead (TPL) Review: SE0015608-SE0015609

SE0015608: Chesterfield 100's Box	
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	98 millimeters (mm)
Diameter	7.89 mm
Ventilation	None
Characterizing Flavor	None
SE0015609: Marlboro 72's Silver Pack Box	
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	72 mm
Diameter	7.89 mm
Ventilation	48%
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	Philip Morris USA Inc.
Report Type	Regular
Product Category	Cigarettes
Product Sub-Category	Combusted, Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

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Date: 2020.03.11 11:09:28 -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: 2020.03.11 12:46:46 -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:

SE0015608: Chesterfield 100's Box	
Product Name	Chesterfield 100's Box
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	98 mm
Diameter	7.89 mm
Ventilation	None
Characterizing Flavor	None
SE0015609: Marlboro 72's Silver Pack Box	
Product Name	Marlboro Silver Pack Box
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	83 mm
Diameter	7.89 mm
Ventilation	46%
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On December 16, 2019, FDA received two SE Reports from Altria Client Services LLC, on behalf of Philip Morris USA Inc. On December 20, 2019, FDA issued an Acceptance letter. On January 2, 2020, FDA issued a Correction letter with a revised new tobacco product name for SE0015608.

1.3. SCOPE OF REVIEW

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

2. REGULATORY REVIEW

Regulatory reviews were completed by Grace Kaiyuan on December 20, 2019.

The reviews conclude that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The predicate tobacco products in SE0015608 and SE0015609 were determined to be substantially equivalent by FDA under SE0014818 and SE0012351[1], respectively. Therefore, the predicate tobacco products are eligible predicate tobacco products.

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 dated February 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

A chemistry review was completed by Scott Wasdo on February 10, 2020. On March 5, 2020, an addendum review was completed by Scott Wasdo

The chemistry reviews conclude 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 reviews identified the following differences:

- A lower total quantity of tobacco filler (SE0015609 only)
- A higher quantity of (b) (4) in the cigarette paper
- A lower quantity of (b) (4) in the cigarette paper
- A different ratio and quantity of (b) (4) in the cigarette paper (SE0015608 only)
- A higher quantity of (b) (4) in the cigarette paper (SE0015609 only)
- (b) (4) cigarette paper banding instead of (b) (4) cigarette paper banding (SE0015608 only)

[1] The predicate tobacco product in SE0014818 is Basic Full Flavor 100's Box, a grandfathered tobacco product (GF1200070). The predicate tobacco product in SE0012351 is Marlboro Ultra Lights Box, a grandfathered tobacco product (GF1200102). SE0012351 was previously submitted as SE0009430, respectively, which received an SE order on June 16, 2015. After receiving an SE order, the applicant notified FDA that there were errors in the ingredient information submitted due to miscalculations. The applicant provided revised ingredient quantities and calculations (see TC0001329). FDA reviewed the information and determined that the changes created distinctly different new and predicate tobacco products and that submission of a new SE Report was required. The applicant subsequently submitted SE0012351, which they certified was identical to SE0009430, with the exception of the revised (b)(4) ingredient quantities. Since the SE order for SE0009430 was based upon incorrect information about the characteristics of the new and predicate tobacco products, these orders were rescinded. In addition, because the information in both sets of SE Reports (other than the ingredient information as noted by the applicant) was identical, a decision was made to duplicate the FDA work products from SE0009430 in the official archive and the Office of Science database. As a result, the scientific reviews SE0012351 reference SE0009430. The chemistry review was the only new scientific review that was conducted for SE0012351 to analyze the revised ingredient information from the applicant.

- A lower quantity of (b) (4) and removal of (b) (4) in the cigarette paper banding (SE0015609 only)
- A lower quantity of ingredients in filter tow, plasticizer and plug wrap (SE0015609 only)
- Analytically non-equivalent decrease in (b) (4) (16%; ISO) and increase in tar (9%; CI) (SE0015609 only)

The new tobacco product in SE0015608 uses the same tobacco filler and filter ingredients (tow, plasticizer, and plug wrap) as the corresponding predicate and grandfathered (GF) tobacco products but has different cigarette paper and tipping ingredients. In particular, when compared to the predicate tobacco product, the new tobacco product cigarette paper uses a higher quantity of (b) (4), a lower quantity of (b) (4), different quantities of (b) (4) (burn rate modifiers) and uses different banding ingredients. While the differences in tipping paper ingredients are not expected to affect user exposure to potential toxicants, the differences in cigarette paper ingredients may cause the new tobacco product to have a different burn rate and smoke profile than that of the corresponding predicate tobacco product.

For the new and predicate tobacco products in SE0015608, the applicant provided smoke yields measured under ISO (International Organization for Standardization) and CI (Canadian Intense) conditions for tar, nicotine, CO (TNCO) and relevant harmful and potentially harmful constituents (HPHCs) that are likely to be altered by the reported ingredient differences [e.g., acetaldehyde, formaldehyde, 1,3-butadiene, benzene, toluene and benzo[a]pyrene (B[a]P)]. Smoke yields for all measured toxicants from the new tobacco product were analytically equivalent to the corresponding yields from the predicate tobacco product. Since the HPHCs tested were suitable to capture any effects the ingredient differences may have on smoke chemistry, this data was suitable to demonstrate that the ingredient differences between the new and corresponding predicate products do not cause the new tobacco product in SE0015608 to raise different questions of public health.

Compared to the corresponding predicate tobacco product, the new tobacco product in SE0015609 has differences in the tobacco filler, cigarette paper ingredients and filter ingredients. The tobacco fillers used in the new and predicate tobacco products have similar tobacco blends and non-tobacco ingredients, but the new tobacco product uses 5.6% less tobacco filler and has a correspondingly lower quantity of the non-tobacco filler ingredients. The cigarette paper used in the new tobacco product has a higher quantity of (b) (4) a reduction in (b) (4) and removal of (b) (4), different banding ingredients, lower quantities of (b) (4), and higher quantities of (b) (4) The new tobacco product filter has less tow, plasticizer and plug wrap than that of the predicate tobacco product.

Since the new tobacco product in SE0015609 combusts a smaller quantity of tobacco than the predicate tobacco product and there are no consequential differences in the tobacco blend, the tobacco blend differences 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. However, the cigarette paper and filter ingredient differences could cause the new tobacco product to have a different burn rate and lower filter efficiency than the predicate tobacco product. This could, in turn, alter the relative smoke chemistries of the new and predicate tobacco products. In particular, these ingredient differences could cause the new tobacco

product to generate higher levels of carbonyls, polyaromatic hydrocarbons (PAHs) and other combustion products.

The applicant provided smoke yields for TNCO and relevant HPHCs measured under ISO and CI conditions for the new and predicate tobacco products in SE0015609. With the exception of tar measured under CI conditions, the smoke yields of all measured toxicants including CO, benzene, acetaldehyde, formaldehyde, nicotine and B[a]P generated by the new tobacco product were analytically equivalent to or lower than those generated by the predicate tobacco product. The HPHCs tested were suitable to capture any effects the reported ingredient differences may have on smoke chemistry. As a result, this data was suitable to demonstrate that the ingredient differences between the new and corresponding predicate tobacco products do not cause the new tobacco product in SE0015609 to raise different questions of public health.

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 February 5, 2020.

The engineering review concludes that the new tobacco product in SE0015609 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 no key engineering differences for SE0015608 and the following differences for SE0015609:

- Decrease in overall cigarette length
- Decrease in tobacco filler mass
- Increase in cigarette paper band porosity
- Decrease in cigarette paper band width
- Increase in filter total denier
- Decrease in filter denier per filament
- Decrease in filter pressure drop
- Decrease in filter length
- Decrease in tipping paper length
- Difference in tobacco amount on a per cigarette basis

As a result of the design parameter information provided plus the design parameters covered by a certification statement, no key differences were identified by engineering for SE0015608. Therefore, the new tobacco product in SE0015608 does not raise different questions of public health from an engineering perspective. In SE0015609, differences in the following design parameters could impact mainstream smoke yields of TNCO and B[a]P: overall cigarette length, tobacco filler mass, cigarette paper band porosity, cigarette paper band width, filter total denier, filter denier per filament, filter pressure drop, filter length, tipping paper length, and differences in tobacco amount on a per cigarette basis (mg/cigarette). These differences do not raise

different questions of public health from an engineering perspective and the evaluation of mainstream smoke yields of TNCO and B[a]P is deferred to chemistry.

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 an engineering perspective.

4.3. TOXICOLOGY

A toxicology review was completed by Theresa Thekkudan on February 4, 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:
  - SE0015608 and SE0015609
    - (b) (4) replaced with (b) (4)
  - SE0015608
    - Added (b) (4)
    - Increased (b) (4) (↑ 96%)
  - SE0015609
    - Added (b) (4)
    - Increased (b) (4) (↑ 60%), (b) (4) (↑ 60%) and (b) (4) (↑ 30%)
- HPHCs
  - SE0015609
    - Carbon monoxide (CO) is analytically inequivalent and decreased (↓16%) under ISO regimen
    - Tar is analytically inequivalent and increased (↑ 9%) under CI regimen

For both SE Reports, there are changes in the cigarette paper in the burned portion of the new tobacco products compared to the corresponding predicate tobacco products. In SE0015608, (b) (4) are added, and (b) (4) is increased in the cigarette paper of the new tobacco product compared to the predicate tobacco product. In SE0015609, (b) (4) is added, and (b) (4) are increased. In addition, in both SE Reports, (b) (4) in the predicate tobacco products is replaced with (b) (4) in the new tobacco products. The added or increased cigarette paper ingredients may pyrolyze to form acetaldehyde, acrolein, B[a]P, benzene, 1,3-butadiene, CO, or formaldehyde in mainstream smoke (MSS).

For both SE Reports, the applicant provided smoke HPHC data including the HPHCs listed above, under ISO and CI regimens. In SE0015608, all the reported HPHC yields of the new tobacco product are analytically equivalent to the predicate tobacco product by a two-one sided t-test

(TOST) analysis. In SE0015609, except CO and tar, all the HPHC yields are analytically equivalent in the new and predicate tobacco products. CO is analytically inequivalent and decreased via ISO regimen, and analytically equivalent via CI regimen in the new tobacco product compared to the predicate tobacco product. In addition, although tar is increased, the applicant has provided an extensive list of HPHC yields which are more direct indicators of exposure to MSS toxicants. All the reported HPHC yields, including PAHs such as benzene, toluene, isoprene, and B[a]P, are either equivalent or decreased in the new tobacco product compared to the predicate tobacco product. Therefore, the tar increase is unlikely to raise different questions of public health from a toxicological perspective. Consequently, in both SE Reports, changes in the cigarette paper ingredients do not 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

An environmental review was completed by Rudaina H. Alrefai-Kirkpatrick on January 17, 2020.

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on February 11, 2020. The FONSI was supported by an environmental assessment prepared by FDA on February 10, 2020.

6. CONCLUSION AND RECOMMENDATION

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

- Design changes (SE0015609 only)
  - Decrease in overall cigarette length
  - Decrease in tobacco filler mass
  - Increase in cigarette paper band porosity
  - Decrease in cigarette paper band width
  - Increase in filter total denier
  - Decrease in filter denier per filament
  - Decrease in filter pressure drop
  - Decrease in filter length
  - Decrease in tipping paper length
  - Difference in tobacco amount on a per cigarette basis
  - A lower quantity of ingredients in filter tow, plasticizer and plug wrap

- Cigarette paper ingredient changes:
  - SE0015608 and SE0015609
    - [redacted] replaced with [redacted]
    - A lower quantity of [redacted] in the cigarette paper
  - SE0015608
    - Added [redacted]
    - Different ratio of [redacted] and [redacted]
    - Increased [redacted]
  - SE0015609
    - Added [redacted]
    - Increased [redacted]
    - Lower quantity of [redacted] banding
- Harmful and Potentially Harmful Constituents (HPHCs)
  - SE0015609
    - 16% decrease in CO under ISO regimen
    - 9% increase in tar under CI regimen

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. The applicant provided a certification statement for SE0015608. The new tobacco product in SE0015608 uses the same tobacco filler and filter ingredients (tow, plasticizer, and plug wrap) as the corresponding predicate tobacco product but has different cigarette paper and tipping ingredients. Compared to the corresponding predicate tobacco product, the new tobacco product in SE0015609 has differences in the tobacco filler and many other design parameters, as well as differences in cigarette paper ingredients and filter ingredients. For both SE Reports, there are changes in the cigarette paper in the burned portion of the new tobacco products, compared to the corresponding predicate tobacco products. The added or increased cigarette paper ingredients may pyrolyze to form a number of HPHCs in MSS. In addition, changes to design parameters in SE0015609 may affect MSS yields. For both the SE Reports, the applicant provided smoke HPHC data for several HPHCs, under ISO and CI regimens. In SE0015608, all the reported HPHC yields of the new tobacco product are analytically equivalent to the predicate tobacco product by a TOST analysis. Therefore, the differences in characteristics between the new and predicate tobacco products in SE0015608 do not cause the new tobacco product to raise different questions of public health. In SE0015609, except CO and tar, all the HPHC yields are analytically equivalent in the new and predicate tobacco products. As explained in section 4.3, differences in CO and tar yields do 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 in SE0015609 do not cause the new tobacco product to raise different questions of public health. 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.

The predicate tobacco products were previously determined to be substantially equivalent by FDA under SE0014818 and SE0012351.

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 products in SE0015608 and SE0015609 were previously determined to be substantially equivalent by FDA under SE0014818 and SE0012351, respectively. Comparison of the new tobacco products to the grandfathered tobacco products (Basic Full Flavor 100's Box [GF1200070] in SE0014818 and Marlboro Ultra Lights Box [GF1200102] in SE0012351) reveals that the new tobacco products have the following differences in characteristics from Basic Full Flavor 100's Box and Marlboro Ultra Lights Box, the grandfathered tobacco products:

- SE0015608
  - A higher quantity of (b) (4) in the cigarette paper
  - A lower quantity of (b) (4) in the cigarette paper
  - (b) (4) cigarette paper banding instead of (b) (4) cigarette paper banding
- SE0015609
  - A higher quantity of (b) (4) in the cigarette paper
  - A lower quantity of all tobacco subtypes (e.g., (b) (4)) in the filler except for (b) (4), which is present in approximately the same quantity as in the corresponding grandfathered (GF) tobacco product
  - A lower quantity of (b) (4) in the cigarette paper
  - A higher quantity of (b) (4) burn rate modifiers (b) (4) in the cigarette paper
  - A lower quantity of ingredients in filter tow, plasticizer and plug wrap

A certification statement provided by the applicant in SE0014818 states that the predicate tobacco product and the corresponding grandfathered tobacco product (GF1200070) have identical cigarette paper and tobacco filler. In addition, no key design changes were identified when comparing the new and GF tobacco products. Therefore, the key differences noted between the new and predicate tobacco product in SE0015608 are the same differences as those between the new and corresponding GF tobacco product. Therefore, as explained above, these differences do not cause the new tobacco product in SE0015608 to raise different questions of public health.

The differences in characteristics listed above regarding the difference in tobacco subtypes, are the same differences in characteristics identified for the new and grandfathered tobacco products in SE0012351. Therefore, these differences do not cause the new tobacco product in SE0015609 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in the quantities of (b) (4) burn rate modifiers, and quantity of (b) (4) filter tow, plasticizer, and plug wrap between the new tobacco product in SE0015609 and the grandfathered tobacco product does not cause the new tobacco product to raise different questions of public health. Therefore, whether comparing the new tobacco product in SE0015609 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 SE0015608 and SE0015609, as identified on the cover page of this review.