Technical Project Lead (TPL) Review:

SE0013909, SE0013910, SE0013911, SE0014710, SE0014711, and SE0014712

SE0013909: Marlboro Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 1
SE0013910: Marlboro 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 1
SE0013911: Marlboro 100's Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 1
SE0014710: Marlboro Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 2
SE0014711: Marlboro 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes

Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 2
SE0014712: Marlboro 100's Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
Additional Properties	Filter Tow 2
Common Attributes of SE Reports	
Applicant	PMUSA
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Todd L. Cecil -S
Digitally signed by Todd L. Cecil -S
Date: 2018.05.23 10:18:40 -04'00'

Todd L. Cecil, Ph.D.
Associate Director
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: 2018.05.23 10:49:45 -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:

SE0013909: Marlboro Soft Pack	
Product Name	Marlboro Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
SE0013910: Marlboro 100's Soft Pack	
Product Name	Marlboro 100's Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
SE0013911: Marlboro 100's Box	
Product Name	Marlboro 100's Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
SE0014710: Marlboro Soft Pack	
Product Name	Marlboro Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
SE0014711: Marlboro 100's Soft Pack	
Product Name	Marlboro 100's Box
Package Type	Hard Pack

Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None
SE0014712: Marlboro 100's Box	
Product Name	Marlboro 100's Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.9 mm
Ventilation	15%
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

FDA received three SE Reports (SE0013909, SE0013910 and SE0013911) from PMUSA on February 9, 2017. On March 1, 2017, FDA issued Acknowledgment letters for all STNs listed above. On March, 24, 2017, FDA received an amendment (SE0013985) containing a correction to the original SE Report for SE0013911 and an amendment (SE0013990) containing updates to the grandfathered predicate tobacco products for all STNs. On May 11, 2017, FDA issued an Advice/Information Request (A/I) letter. FDA received amendment (SE0014195) containing a response to the A/I letter on July 7, 2017. On September 29, 2017, FDA issued a Preliminary Finding (Pfind) letter. FDA received an amendment (SE0014392) containing a response to the Pfind letter on October 27, 2017. On January 24, 2018, FDA issued another Pfind letter. FDA received an amendment (SE0014549) containing a response to the Pfind letter on February 22, 2018. On April 25, 2018, FDA received an unsolicited amendment (SE0014647) which provided a correction to SE0014392. The amendment was received after the scientific review was completed. The TPL reviewed the amendment and found that the changes provided did not change the chemistry or toxicology review and therefore did not affect the TPL Review. On May 9, 2018, the TPL determined the SE reports received on February 9, 2017, contained different filter materials, specifically filter tow, for the new tobacco products. On May 21, 2018, a memorandum was finalized to capture the breakout of new products for the additional unique identifier of the filter tow. New STNs (SE0014710 – SE00 14712) were created for the tobacco products with filter tow 2. All amendments and SE Reports described below for SE0013909-SE0013911 are also applicable to SE0014710-SE0014712, respectively.

Product Name(s)	SE Report	Amendments
Marlboro Soft Pack	SE0013909	SE0013990 SE0014195 SE0014392 SE0014549 SE0014647
Marlboro 100's Soft Pack	SE0013910	
Marlboro 100's Box	SE0013911	SE0013985 SE0013990 SE0014195 SE0014392 SE0014549 SE0014647
Marlboro Soft Pack	SE0014710	SE0013990 SE0014195 SE0014392 SE0014549 SE0014647
Marlboro 100's Soft Pack	SE0014711	
Marlboro 100's Box	SE0014712	SE0013985 SE0013990 SE0014195 SE0014392 SE0014549 SE0014647

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 Iqra Javaid on February 28, 2017, for SE0013909, and March 1, 2017, for SE0013910, and SE0013911[1].

The final reviews conclude that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed reviews to determine whether the applicant established that the predicate tobacco products are grandfathered products (i.e., were commercially marketed other than exclusively in test markets as of February 15, 2007). The OCE review dated April 13, 2017, concludes that the evidence submitted by the applicant is adequate to

[1] The regulatory reviews completed for SE00139●9SE0012911 are applicable to SE0014710SE●●14712 as documented in the memo to file dated May 21, 2018.

demonstrate that the predicate tobacco products are grandfathered and, therefore, are eligible predicate tobacco products[2].

OCE also completed reviews to determine whether the new tobacco products are 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 30, 2018, 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 Lida Oum on April 4, 2017, and Jianping Gong on September 14, 2017, and December 12, 2017.

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:

- Increase in (b) (4) by 14%-16%
- Addition o (b) (4) (b) (4) mg/cig) in FSC cigarette paper
- Decrease in (b) (4) (b) (4) mg/cig) by 29%

The increase in (b) (4) may lead to increases in NNN and NNK in the new tobacco products. However, because to the small amount of (b) (4) added per cigarette, the effects of the pyrolysis to form NNN or NNK are likely not measurable. Therefore, the increase in (b) (4) does not cause the new tobacco products to raise different questions of public health. The new tobacco products contain (b) (4) (b) (4) mg/cig) in FSC cigarette paper, but the predicate tobacco products do not. Increases (b) (4) may lead to increases in B[a]P, acetaldehyde and benzene. The applicant provided measurements of benzo[a]pyrene, acetaldehyde, and benzene in the new and surrogate predicate tobacco products and the differences were within the error of the analytical error. A reduction in the amount of (b) (4) in the cigarette paper for the new tobacco products could decrease the burn rate and increase the yields of TNCO in smoke. The applicant provided measurements of TNCO in the new and surrogate predicate tobacco products and all of the differences were within the error of the analytical error. 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.

[2] In addition, OCE completed addendum reviews on April 26, 2018 to add the characterizing flavor to the April 13, 2017 reviews. The addendums do not change the conclusion of the initial determination.

4.2. ENGINEERING

Engineering reviews were completed by Rashele Moore on April 20, 2017, and Michael Morschauser on September 8, 2017, and December 12, 2017.

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

- Increased cigarette paper band width
- Decreased cigarette paper band porosity

The new tobacco products have increased cigarette paper band width and decreased band porosity. The combination of these parameters would lead to a greater portion of the cigarette paper coated by a lower porosity band, which may lead to an increase TNCOs. However, the applicant demonstrated that the changes do not have a significant effect on the overall porosity of the cigarette paper. 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 and engineering perspective.

4.3. TOXICOLOGY

Toxicology reviews were completed by Sheila Healy on May 3, 2017, September 22, 2017, and December 29, 2017.

The final 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:

- Amount of (b) (4) increased, attributed to the 35% increase in (b) (4))
- Amount of (b) (4) increased
- (b) (4) are added to cigarette paper
- (b) (4) is added to the monogram ink (alternate 1)
- (b) (4) are increased in the monogram ink (alternate 2)

An increase in (b) (4) tobacco may lead to increases in TNCOs, NNN, and NNK smoke yields from the new tobacco products. The applicant provided measured values for each of these HPHCs, and all were either approximately the same or lower in the new tobacco products compared to the corresponding surrogate predicate tobacco product. Based on the information provided, the changes in tobacco blend (b) (4)) will not cause the new tobacco products to raise different questions of public health. The measured HPHC yields also indicated that the increase (b) (4) do not cause the new tobacco products to raise different questions of public health. The pyrolysis of (b) (4) and (b) (4) have been shown to generate HPHCs, including

benzo[a]pyrene, acetaldehyde and benzene. The applicant provided smoke yields of benzo[a]pyrene, acetaldehyde and benzene in the new and surrogate predicate tobacco products. Benzo[a]pyrene, acetaldehyde and benzene smoke yields were not significantly different under either the ISO and Canadian Intense smoking regimens. Therefore, the addition of (b) (4) and (b) (4) to the new tobacco products will not raise different questions of public health. The predicate tobacco product was manufactured using two different monogram inks. The effects of both ink changes were evaluated in combination. Because the monogram inks are not expected to be combusted, volatilized or released during cigarette consumption, consumer exposure to ingredients of monogram inks while smoking is expected to be minimal. Therefore, changes in the inks are low enough that it will not cause the new tobacco products 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 toxicology perspective.

4.4. SOCIAL SCIENCE

A social science review was completed by Jennifer Bernat on December 1, 2017.

The social science review concludes that the new tobacco products have a different characteristic related to consumer use and perception compared to the corresponding predicate tobacco products, but the difference does not cause the new tobacco products to raise different questions of public health. The review identified the following difference:

- Increase in cigarette length (1%) (For SE0013909 and SE0014710 only)

The currently available evidence suggests that changes in the length of the cigarette stick may influence consumer perceptions of the product. However, at this time, there is insufficient scientific evidence on the influence of the length of cigarettes on consumer perceptions to indicate that a 1% increase in length would cause the new tobacco products to raise different questions of public health from a social science perspective. Therefore, the difference in characteristics between the new and corresponding predicate tobacco products does not cause the new tobacco products to raise different questions of public health from a social science perspective.

5. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on May 21, 2018. The FONSI was supported by an environmental assessment prepared by FDA on May 21, 2018.

6. CONCLUSION AND RECOMMENDATION

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

- Addition of (b) (4) in FSC cigarette paper
- Decrease in (b) (4) in the cigarette paper
- Increased cigarette paper band width
- Decreased cigarette paper band porosity
- Increase in (b) (4)
- Increases i (b) (4)
- Addition of (b) (4) to the monogram ink ((alternate 1)
- Increase in (b) (4) in the monogram ink (alternate 2)
- Increase in cigarette length (1%) (For SE0013909 and SE0014710 only)

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. The new tobacco products each contain differences in ingredients which may lead to increases in TNCOs and other HPHCs. The addition of (b) (4), (b) (4) may lead to increases in B[a]P, carbonyls, and benzene. The applicant provided measured HPHCs in smoke for the new and corresponding surrogate predicate tobacco products that demonstrated that these HPHCs in the new tobacco products were either lower or similar to the corresponding surrogate predicate tobacco products. Therefore, the differences in (b) (4) do not cause the new tobacco product to raise different questions of public health. The decrease in (b) (4) in the cigarette paper, decrease in the cigarette paper band porosity, increase in the cigarette paper band width, and increase in cigarette length (For SE0013909 and SE0014710 only) may each lead to an increase in TNCOs. The applicant provided TNCO values for the new tobacco products that are similar to that of the corresponding surrogate predicate tobacco product. Therefore, the differences in the (b) (4) content, the cigarette paper band width, cigarette paper band porosity, and cigarette length to not cause the new tobacco product to raise different questions of public health. An increase in (b) (4) may lead to increases in TNCOs in the smoke yield from the new and corresponding surrogate predicate tobacco products. The applicant provided measured values for TNCOs from the new tobacco products were similar to those from the corresponding surrogate predicate tobacco product. Therefore, the differences in the (b) (4) do not cause the new tobacco product to raise different questions of public health. The increased cigarette length, (b) (4) and the monogram inks may each inherently raise different questions of public health. However, each of these ingredients is present at levels small enough that neither they nor their pyrolysis products 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 meet statutory requirements because it was determined that they are grandfathered products (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

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 SE0013909, SE0013910, SE0013911, SE0014710, SE0014711, and SE0014712, as identified on the cover page of this review.