Technical Project Lead (TPL) Review: SE0014912, SE0014913, SE0014914 and SE0014915

SE0014912: Merit Blue Pack 100's Box	
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter[1]	7.89 mm
Ventilation	55%
Characterizing Flavor	None
SE0014913: Marlboro Black Label Box	
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.89 mm
Ventilation	14%
Characterizing Flavor	None
Additional Property	Tipping Paper - 2
SE0014914: L&M Turkish Blend Box	
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.89 mm
Ventilation	23%
Characterizing Flavor	None
SE0014915: L&M Turkish Blend 100's Box	
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter[1]	7.64 mm
Ventilation	17%
Characterizing Flavor	None

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

Common **Attributes of SE Reports**	
Applicant	Phillip Morris USA
Report Type	Regular
Product Category	Cigarettes
Product Sub-Category	Combusted, filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Melissa Mcculloch -S

Digitally signed by Melissa Mcculloch -S
Date: 2019.01.24 16:54:37 -05'00'

Melissa McCulloch, Ph.D.
Senior Regulatory Scientist
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)

Matthew R. Holman -S

Digitally signed by Matthew R. Holman -S
Date: 2019.01.24 17:17:38 -05'00'

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:

SE0014912: Merit Blue Pack 100's Box	
Product Name	Merit Ultra Lights 100's Box
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter[1]	7.89 mm
Ventilation	55%
Characterizing Flavor	None
SE0014913: Marlboro Black Label Box	
Product Name	Marlboro Blend No. 27 Box
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.89 mm
Ventilation	14%
Characterizing Flavor	None
SE0014914: L&M Turkish Blend Box	
Product Name	Players Kings Box
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	83 mm
Diameter[1]	7.89 mm
Ventilation	23%
Characterizing Flavor	None
SE0014915: L&M Turkish Blend 100's Box	
Product Name	Players 100's Box
Package Type	Hard pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter[1]	7.64 mm
Ventilation	17%
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On October 29, 2018, FDA received four SE Reports (SE0014912 - SE0014915), from Altria Client Services (ALCS) on behalf of Philip Morris USA Inc. FDA issued an Acknowledgement letter on November 5, 2018.

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 Ester Hatton on November 5, 2018.

The 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 in the United States other than exclusively in test markets as of February 15, 2007). The OCE reviews dated November 29, 2018, conclude that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco products are grandfathered and, therefore, are eligible predicate tobacco products.

OCE also completed a review to determine whether the new tobacco products are 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 January 10, 2019, 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 Selena Russell on December 11, 2018.

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

Tipping paper:

- (b) (4) decreased 64% – 81% ((b) (4) mg/cigarette)
- (b) (4) increased 185% – 211% ((b) (4) mg/cigarette)

Inks:

- Decreased 30% – 31% ((b) (4) mg/cigarette) in SE0014912 and SE0014913
- Increased 10% – 12% ((b) (4) mg/cigarette) in SE0014914 and SE0014915

Total cigarette weight:

- Decreased 0.09% (0.9 and 0.8 mg/cigarette, respectively) in SE0014912 and SE0014913
- Increased 0.02% (0.2 mg/cigarette) in SE0014914 and SE0014915

Tipping paper adhesive:

- Addition of (b) (4) mg/cigarette (b) (4) in SE0014913

The applicant certified that the characteristics of the new and predicate tobacco products are identical in materials, ingredients, design features, heating source, or any other feature of the new product, except for the non-tobacco ingredients, tipping papers, tipping inks, tipping ink extenders, and tipping paper adhesive. Except for (b) (4), most ingredient differences are either decreases or very small increases (below (b) (4) mg/cigarette). The 185% – 211% increase in (b) (4) quantity in the tipping paper of the new tobacco products ((b) (4) mg/cigarette) was deferred to toxicology for evaluation and is discussed in Section 4.2 of this review. All ingredient differences are in non-combusted components. Furthermore, the new and corresponding predicate tobacco products have identical ventilation; therefore, the differences are not expected to affect smoke chemistry, including the production of harmful and potentially harmful constituents (HPHCs). 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. TOXICOLOGY

A toxicology review was completed by Ines Pagan on December 19, 2018.

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

- Several minor ingredient additions and increases (less than [(b) (4)] /cigarette) to the tipping paper, inks, and ink extenders in the cigarette filter
- [(b) (4)] increased 185% – 211% ([(b) (4)] mg/cigarette) in the tipping paper
- [(b) (4)] was added ([(b) (4)] mg/cigarette) to the tipping adhesive in SE0014913[2]

The toxicology review determined that all ingredient differences occur in the surface tipping components of the cigarette that are not expected to be heated or burned; therefore, they are unlikely to pyrolyze or contribute to the inhaled mainstream smoke of the cigarette. Further, most ingredient additions and increases associated with these tipping material modifications are very small, below [(b) (4)] mg/cig (except for [(b) (4)] and would not result in oral or dermal exposures. Therefore, the ingredient additions and increases to the tipping paper, inks, and ink extenders do not cause the new tobacco product to raise different questions of public health from a toxicology perspective. [(b) (4)] is a potential hepatotoxicant and neurotoxicant depending on its physical form and dose, which determines its bioavailability and reactivity. More specifically, in its nanoparticle form, increases in reactive oxygen species (ROS) production and oxidative products (i.e., lipid peroxidation) have been identified with [(b) (4)] exposure, which are suspected to comprise a key mechanism for associated adverse biological effects. Further, oral exposure (30 to 60-days) to ultrafine or nanoparticle sized [(b) (4)] was found to cause hepatotoxicity and neurotoxicity in mice, with toxicity apparent at the lowest dose tested (i.e., 5 mg/kg). The applicant provided information that the median particle diameter of [(b) (4)] in the tipping paper is 560 nm and 340 nm in the tipping inks. Given the reported particle sizes, the [(b) (4)] is unlikely to migrate outside the cellulose matrix, thus oral exposure is not a concern. Therefore, the increase in [(b) (4)] does not cause the new tobacco product to raise different questions of public health from a toxicology perspective. [(b) (4)] is an added ingredient in the tipping adhesive of the new tobacco product in SE0014913. It has been demonstrated that very low amounts of [(b) (4)] may cause adverse health effects.[3] The applicant provided a statement from the supply vendor that the [(b) (4)] is volatile and will evaporate from the tobacco product during the drying process. Since the [(b) (4)] will not be present in the solidified adhesive film, its addition to the tipping adhesive of the new tobacco product in SE0014913 does not cause the new tobacco product to raise different questions of public health from a toxicology perspective. Therefore, the differences in characteristics between the new and corresponding predicate tobacco products does not cause the new tobacco product to raise different questions of public health from a toxicology perspective.

5. ENVIRONMENTAL DECISION

An environmental review was completed by Thomas Creaven on November 30, 2018.

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on January 24, 2019. The FONSI was supported by an environmental assessment prepared by FDA on January 24, 2019.

[2] The toxicology review contains a typographical error on page 7, SE0014913 is incorrectly referred to as SE1490013.

[(b) (4)]

6. CONCLUSION AND RECOMMENDATION

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

- (b) (4) decreased 64% – 81% in the tipping paper
- (b) (4) increased 185% – 211% in the tipping paper
- The amount of ink decreased 30% – 31% in SE0014912 and SE0014913
- The amount of ink increased 10% – 12% in SE0014914 and SE0014915
- The total cigarette weight decreased 0.09% in SE0014912 and SE0014913
- The total cigarette weight increased 0.02% in SE0014914 and SE0014915
- Several minor ingredient additions and increases (less than (b) (4) cigarette) to the tipping paper, inks and ink extenders in the cigarette filter
- (b) (4) was added ((b) (4) mg/cigarette) to the tipping adhesive in SE0014913

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. Most ingredient additions and increases associated with these tipping material modifications are very small, below (b) (4) mg/cigarette, except for (b) (4). Further, these tipping materials are not combusted during normal cigarette use and, therefore, changes to their compositions are not expected to affect smoke chemistry, including HPHCs. (b) (4) is a potential hepatotoxicant and neurotoxicant depending on its physical form and dose, which determines its bioavailability and reactivity. The applicant provided information that the median particle diameter of (b) (4) in the tipping paper is 560 nm and 340 nm in the tipping inks, indicating that this chemical compound is not in the ultrafine or nanoparticle form in the tobacco products. Therefore, the increase in (b) (4) does not cause the new tobacco products to raise different questions of public health from a toxicology perspective. Although a small amount of (b) (4) is added to the tipping adhesive in the new tobacco product in SE0014913 (< (b) (4) mg/cigarette), low amounts of (b) (4) can lead to negative health impacts. The applicant provided information that the (b) (4) will evaporate from the tobacco product during the drying process. Since the (b) (4) will not be present in the solidified adhesive film, its addition to the tipping adhesive of the new tobacco product does not cause the new tobacco product to raise different questions of public health from a toxicology perspective. Therefore, the differences in characteristics between the new and corresponding predicate tobacco products does 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 tobacco 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 SE0014912, SE0014913, SE0014914 and SE0014915, as identified on the cover page of this review.