FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0015281

SE0015281: Marlboro 100's Box	
Package Type	Hard Pack
Package Quantity	20 Cigarettes
Length	98 millimeters (mm)
Diameter	7.89 mm
Ventilation	15%
Characterizing Flavor	None
Common Attributes of SE Report	
Applicant	Philip Morris USA Inc.
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue a Substantially Equivalent (SE) order.	

Technical Project Lead (TPL):

Digitally signed by Jeannie H. Jeong-im -S
Date: 2020.03.13 09:41:04 -04'00'

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: 2020.03.13 10:19:47 -04'00'

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

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BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco product:

SE0015281: Marlboro 100's Box	
Product Name	Marlboro 100's Box
Package Type	Box
Package Quantity	20 Cigarettes
Length	98 mm
Diameter	7.89 mm
Ventilation	15%
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On June 28, 2019, FDA received an SE Report from Altria Client Services (ALCS) on behalf of Philip Morris USA Inc. (PMUSA). On July 9, 2019, FDA issued an Acknowledgement letter.

On September 9, 2019, FDA issued a Deficiency letter with response due date of March 20, 2020. On December 20, 2019, FDA received the response to the Deficiency letter (SE0015627)

Product Name	SE Report	Amendments
Marlboro 100's Box	SE0015281	SE0015627

1.3. SCOPE OF REVIEW

This review captures all regulatory, compliance, and scientific reviews completed for this SE Report.

REGULATORY REVIEW

A regulatory review was completed by Ester Hatton on July 09, 2019.

The review concludes that the SE Report is administratively complete.

On December 20, 2019, FDA received a response (SE0015627) to the Deficiency letter issued on September 9, 2019. The Completeness review was completed on December 23, 2019. The Applicant provided response on all the deficiencies.

COMPLIANCE REVIEW

The predicate tobacco product in SE0015281 was determined to be substantially equivalent by FDA under SE0014712. 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 new tobacco product is 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 February 4, 2020 concludes that the new tobacco product is in compliance with the FD&C Act.

SCIENTIFIC REVIEW

Scientific reviews were completed by the Office of Science (OS) for the following disciplines:

1.4. CHEMISTRY

Chemistry reviews were completed by Robert F. Gahl on August 16, 2019 and February 7, 2020.

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

- Difference in Tipping paper:
  - Addition of (b) (4) to tipping adhesive ((b) (4) mg/cigarette (b) (4)
- Differences in the Cigarette Paper:
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette) to the FSC bands
  - 25% increase in (b) (4) mg/cigarette)
- 1,043% increase in (b) (4) mg/cigarette)

The applicant stated that the only changes to the new tobacco product compared to the predicate tobacco product was the addition of (b) (4) mg/cigarette of (b) (4) to the tipping adhesive and minor differences in the cigarette paper and ingredients added to tobacco. The tipping adhesive solvent is (b) (4), and it is part of the cigarette that is not combusted during normal cigarette use. Therefore, the change of tipping adhesive ingredients is not expected to contribute to HPHC smoke yields in the new tobacco product and does not cause the new tobacco product to raise different questions of public health. However, the changes in the cigarette paper include a 25% increase in (b) (4), a 231% increase in (b) (4) additions of (b) (4) and (b) (4), an 8% decrease in FSC band width, and a 125% increase in band porosity as well as a 1,043% increase in (b) (4) that could lead to increases in the level of the following HPHCs in mainstream smoke: tar, nicotine, carbon monoxide, acetaldehyde, acrolein, benzene, crotonaldehyde, formaldehyde, and B[a]P. The

applicant provided complete data sets and method information for the mainstream smoke levels of HPHCs under the ISO and CI regimens. TOST analysis determined that the yields of these HPHCs under the ISO and CI regimens are analytically equivalent. Therefore, the changes in the tipping adhesive, cigarette paper, complex ingredients, and the HPHC smoke data do not cause the new tobacco product to raise different questions of public health from a chemistry perspective.

1.5. ENGINEERING

An engineering review was completed by Ryan Andress on August 16, 2019.

The engineering review concludes that the new tobacco product 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 the following differences:

- 125% higher band porosity
- 8% lower band width

With exception of the cigarette paper, the new and predicate products are identical. There are differences in cigarette paper band porosity and cigarette paper band width. The evaluation of the yields of TNCO and B[a]P is deferred to chemistry. The new product in SE0015281 does not raise different questions regarding public health, from an engineering perspective.

1.6. TOXICOLOGY

Toxicology reviews were completed by Chad N. Broker on August 20, 2019 and Juan M. Crespo-Barreto on February 7, 2020.

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

Toxicology evaluation complete:

- Addition of (b) (4) in tipping adhesive (non-combusted portion)
- Tobacco ingredients
  - (b) (4) mg/cig; ↑1,043%)
  - (b) (4) µg/cig; ↑added)
- Cigarette paper ingredients
  - (b) (4) mg/cig; ↑65.4%)
  - (b) (4) mg/cig; ↑65.4%)
  - (b) (4) mg/cig; ↑added)
  - (b) (4) mg/cig; ↑added)
  - (b) (4) mg/cig; ↓removed)

- Other ingredients
  - [redacted] mg/cig; ↑231.3%)

The applicant reported changes in ingredients added to tobacco and cigarette paper in the new product as compared to the predicate product. Some of these ingredient changes may affect smoke yields of HPHCs such as acetaldehyde, acrolein, benzene, and formaldehyde. The applicant reported yields of nine HPHCs (tar, nicotine, carbon monoxide, acetaldehyde, acrolein, benzene, crotonaldehyde, formaldehyde, and B[a]P) from the new and predicate product in SE0015281 under both ISO and CI smoking regimens. TOST analyses of these data showed that the provided HPHC yields in the new and predicate products of SE0015281 were analytically equivalent. Adequate validation information was provided on the methods. Therefore, these ingredient changes do not cause the new product in SE0015281 to raise different questions of public health from a toxicological perspective.

ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on February 5, 2020. The FONSI was supported by an environmental assessment prepared by FDA on February 5, 2020.

CONCLUSION AND RECOMMENDATION

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

- Difference in Tipping paper:
- Addition of [redacted] to tipping adhesive
- Differences in the Cigarette Paper:
  - Addition of [redacted]
  - Addition of [redacted] to the FSC bands
  - 25% increase in [redacted]
- 1,043% increase in [redacted]
- Addition of [redacted]
- 231% increase in [redacted]
- Addition of [redacted] in the cigarette paper
- Substitution of [redacted] with [redacted] in the cigarette paper

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco product to raise different questions of public health. The [redacted] is added to the tipping paper adhesive. The tipping paper adhesive is not a part of the cigarette that is combusted during normal cigarette use, and not expected to contribute to HPHC smoke yields. However, the changes in the cigarette paper include a substitution of [redacted] with [redacted] 231% increase in [redacted], additions of [redacted] and [redacted], 8% decrease in FSC band width, and 125% increase in band porosity as well as a 1,043% increase in [redacted] and addition of [redacted] that could lead to increases in HPHCs. The applicant provided the level of the following HPHCs in mainstream smoke: tar, nicotine, carbon monoxide, acetaldehyde, acrolein, benzene, crotonaldehyde, formaldehyde, and B[a]P under intense and non-intense smoking

regimens. TOST analyses of these data showed that the provided HPHC yields in the new and predicate products were analytically equivalent. Adequate validation information was provided on the methods. 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 was previously determined to be substantially equivalent by FDA under SE0014712.

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 SE0015281 was previously determined to be substantially equivalent by FDA under SE0014712. Comparison of the new tobacco product to the grandfathered product (Marlboro 100's Box) reveals that the new tobacco product has the following differences in characteristics from Marlboro 100's Box, the grandfathered tobacco product:

- Difference in Tipping paper:
  - Addition of (b) (4) to tipping adhesive
- Differences in the Cigarette Paper
  - Citrate content: 105% increase in (b) (4) removal of (b) (4) and addition of (b) (4)
  - 96% increase in (b) (4) in FSC band
  - 581% increase in (b) (4) in FSC band
  - Removal of (b) (4) in FSC band
  - Addition of (b) (4) in FSC band
- Differences in Cigarette Design
  - 10% increase in filter total denier
- Differences that are not analytically equivalent in mainstream smoke yields of Carbon Monoxide (14% increase by ISO) and Benzo[a]Pyrene (20% decrease by Canadian Intense).

The differences in characteristics listed above, other than the differences in tipping and cigarette papers, are the same differences in characteristics identified for the new and grandfathered tobacco products in SE0015281. Therefore, these differences do not cause the new tobacco product in SE0015281 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in tipping paper adhesive, cigarette paper ingredients, cigarette design (filter total denier), and in MS smoke yields of carbon monoxide and benzo[a]pyrene between the new tobacco product in SE0015281 and the grandfathered tobacco product do not cause the new tobacco product to raise different questions of public health. Therefore, whether comparing the new tobacco product in SE0015281 to the predicate or grandfathered tobacco products, the new tobacco product does not raise different questions of public health.

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 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 product in se0015281, as identified on the cover page of this review.