U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review:

SE0004087, SE0004088, SE0004094, SE0004125, and SE0004173

SE0004087: Basic 100's Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	15 %
Characterizing Flavor	None
SE0004088: Basic Menthol Gold Pack 100's Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	20 %
Characterizing Flavor	Menthol
SE0004094: L&M 100's Box	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	15 %
Characterizing Flavor	None
SE0004125: Basic Menthol Gold Pack 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	20 %
Characterizing Flavor	Menthol
SE0004173: Basic 100's Soft Pack	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	15 %
Characterizing Flavor	None

Common Attributes of SE Reports	
Applicant	Philip Morris USA
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Todd Cecil Digitally signed by Todd Cecil
Date: 2018.04.05 19:33:09
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Todd 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: 2018.04.05 19:47:53 -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:

SE0004087: Basic 100's Box	
Product Name	Basic Full Flavor 100's Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.89 mm
Ventilation	0 %
Characterizing Flavor	None
SE0004088: Basic Menthol Gold Pack 100's Box	
Product Name	Basic Menthol Lights 100s Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99.5 mm
Diameter	7.89 mm
Ventilation	20 %
Characterizing Flavor	Menthol
SE0004094: L&M 100's Box	
Product Name	Marlboro Medium 100s Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98.5 mm
Diameter	7.89 mm
Ventilation	20 %
Characterizing Flavor	None
SE0004125: Basic Menthol Gold Pack 100's Soft Pack	
Product Name	Basic Menthol Lights 100s Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99.5 mm
Diameter	7.89 mm
Ventilation	20 %
Characterizing Flavor	Menthol

SE0004173: Basic 100's Soft Pack	
Product Name	Basic Full Flavor 100s Box
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	98 mm
Diameter	7.89 mm
Ventilation	0 %
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 SE Reports for the tobacco products listed above on January 21, 2012, which was submitted by Altria Client Services Inc. (ALCS) on behalf of Philip Morris USA Inc. (PM USA). FDA acknowledged the SE Reports for SE0004087 SE0004088 and SE0004094 on February 16, 2012, SE0004125 on February 24, 2012, and SE0004173 on April 12, 2012. FDA issued Correction letters on March 6, 2012, to correct the product identification information for SE0004087 SE0004088, SE0004094, and SE0004125. FDA issued Advice/Information (A/I) Request letters for SE0004087 SE0004088 on March 13, 2012, SE0004094 on April 10, 2012, and SE0004125 and SE0004173 on April 20, 2012. On May 10, 2012 (SE0004393, SE0004394, SE0004397, and SE0004399), and June 8, 2012 (SE0004568), FDA received the response to the A/I letter. On March 22, 2013, FDA issued A/I letters. On April 4, 2013, FDA received a 121-days extension request (SE0008140) to allow sufficient time to respond to multiple letters. On April 10, 2013, FDA issued the Extension Granted letter. On September 11, 2013, FDA received a request (SE0009774) to withdraw the cigarette paper #1 from the SE Reports listed above. On September 12, 2013, FDA receive the response to March 22, 2013, A/I request letter (SE0009779, SE0009782, SE0009785, SE0009787, and SE0009789). On September 20, 2013, FDA received amendments (SE0009836, SE0009839, and SE0009840) to update the September 12, 2013, response to the A/I letter for SE Reports SE0004088, SE0004125, and SE0004094. On October 25, 2013, FDA issued a Correction letter to correct the product identification information. On December 3, 2013, FDA requested clarification to the applicant's response to the March 22, 2013, A/I letter. On December 3, 2013, FDA received an amendment (SE0010006) in response to the clarification request. On September 3, 2015, FDA received an amendment (SE0012354) to correct the ingredient table in the original SE Reports. On May 31, 2017, FDA issued a Preliminary Finding (PFind) letter. On June 9, 2017, FDA received a 71-days extension request (SE0014140) to conduct additional HPHC testing in order to provide a complete response to the identified deficiencies. On July 13, 2017, FDA issued an Extension Granted letter. On September 8, 2017, FDA received the response to the PFind letter (SE0014311). On September 21, 2017, FDA received an amendment (SE0014343) to correct the unit of measure for the (b) (4) [redacted] data in the September 8, 2017, response to the PFind letter. On December 7, 2017, FDA issued a PFind letter to request information for the environmental assessment. On January 05, 2018, FDA received the response to the PFind letter (SE0014461). On April 2, 2018, FDA received an amendment (SE0014604) to update the January 5, 2018, response to the PFind

letter. FDA did not review this amendment as the changes do not affect the conclusion of the chemistry or toxicology reviews.

Product Name(s)	SE Report	Amendments
Basic 100's Box	SE0004087	SE0004393, SE0008140, SE0009774, SE0009779, SE0009790, SE0010006, SE0012354, SE0014140, SE0014311, SE0014343, SE0014461, SE0014604
Basic Menthol Gold Pack 100's Box	SE0004088	SE0004394, SE0008140, SE0009774, SE0009782, SE0009790, SE0009836, SE0010006, SE0012354, SE0014140, SE0014311, SE0014343, SE0014461, SE0014604
L&M 100's Box	SE0004094	SE0004568, SE0008140, SE0009774, SE0009785, SE0009790, SE0009840, SE0010006, SE0012354, SE0014140, SE0014311, SE0014343, SE0014461, SE0014604
Basic Menthol Gold Pack 100's Soft Pack	SE0004125	SE0004397, SE0008140, SE0009774, SE0009787, SE0009790, SE0009839, SE0010006, SE0012354, SE0014140, SE0014311, SE0014343, SE0014461, SE0014604
Basic 100's Soft Pack	SE0004173	SE0004399, SE0008140, SE0009774, SE0009789, SE0009790, SE0010006, SE0012354, SE0014140, SE0014311, SE0014343, SE0014461, SE0014604

1.3. SCOPE OF REVIEW

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

2. REGULATORY REVIEW

Completeness reviews were completed by Jonathan Kwan on March 13, 2012 and May 30, 2012 (SE0004087 and SE0004088), April 10, 2012, and June 21, 2012 (SE0004094), and April 20, 2012, and May 30, 2012 (SE0004125 and SE0004173).

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 December 20, 2012, December 3, 2012, and November 30, 2012 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[1].

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 reviews dated November 13, 2017, February 13, 2018, and April 3, 2018, conclude 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 Candice Jongsma on January 31, 2013, Katherine Lovejoy on January 21, 2014, and Abdurrafay Shareef on November 1, 2017.

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

- Lower total tobacco (b) (4)
- Tobacco blend changes
- Menthol increase [SE0004088 and SE0004125]
- Increases in (b) (4) ((b) (4) and (b) (4) ((b) (4) in the filter tow and filter plug wrap [SE0004087 and SE0004173]

[1] Addendum reviews were completed on June 19, 2013 for SE0004087, SE0004088, and SE0004173, to include the package type, length of each cigarette and number of cigarettes per pack for the predicate tobacco products; on June 5, 2013 for SE0004094, to include the package type and size for the predicate tobacco product; on March 16, 2018 for SE0004087, SE0004094, and SE0004173, to include the characterizing flavor for the predicate tobacco products. The conclusion in the addendum reviews did not differ from that in the original OCE reviews.

Tobacco blend changes may change the types and amounts of HPHCs present in the smoke of the new and corresponding predicate tobacco products, while decreases in total tobacco content in a cigarette is likely to reduce all HPHC levels. The applicant reported TSNA smoke data and additional HPHC measurements in smoke for the new and surrogate predicate tobacco products. The HPHCs were reported to be the same or lower in the smoke of the new tobacco products than the smoke of the surrogate tobacco products. The results were recorded using appropriate analytical techniques and therefore, the change in tobacco blend and other ingredients added or increased in the new tobacco products do not raise different questions of public health from a chemistry perspective. The new tobacco products were also reported to contain more menthol in the new product compared to predicate product. The applicant provided mainstream smoke data showing lower menthol levels in the new tobacco products compared to the corresponding predicate tobacco products. Thus, the menthol content does not cause the new tobacco products to raise different questions of public health related to product composition. The changes to the filter tow and filter plug wrap do not cause the new tobacco products to raise different questions of public health related to product composition because they are in a non-combusted portion of the cigarette and therefore, are not likely to increase the HPHC content.

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 composition.

4.2. ENGINEERING

Engineering reviews were completed by Christian Coyle on February 12, 2013, and James Melchiors on January 21, 2014, and November 7, 2017.

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

- All of the SE Reports: puff count is lower
- SE0004087 and SE0004173:
  - The cigarette draw resistance, tobacco filler mass, cigarette paper base paper porosity, and filter pressure drop is lower
  - Filter ventilation was added
  - The filter is longer and the tipping paper is correspondingly longer
- SE0004094:
  - The cigarette draw resistance is higher
  - The cigarette paper base paper porosity and the filter ventilation are lower

The change in puff count may lead to a change in the exposure to HPHCs. However, the differences in the puff count were small and are unlikely to result in HPHC changes. Decreases in tobacco filler mass is likely to lead to lower HPHC exposure and therefore does not raises different questions of public health. Increases in the filter tip length and associated filter paper length are not expected to result in an increase in HPHC exposure, provided that the filter

pressure drop is not substantially higher. The filter pressure drop is reported to be the same or lower as is the cigarette paper base paper porosity. The decreases in the filter pressure drop and cigarette paper base paper porosity do not raise a risk of higher exposure and are therefore do not raise different questions of public health. Finally, the introduction of ventilation may lead to a decrease in HPHC yields and therefore does not raise different questions of public health. SE0004094 is reported to have a higher cigarette draw resistance which is associated with the decrease in cigarette paper base paper porosity and filter ventilation. These differences are likely to result in changes in the TNCO and particulate-borne HPHCs. The applicant provided data to demonstrate that the TNCO and particulate-borne HPHCs do not increase and therefore 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 related to product design.

4.3. TOXICOLOGY

Toxicology reviews were completed by Hans Rosenfeldt on February 25, 2013, Sheila Healy on March 29, 2017, and Shaji Theodore on November 6, 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 related to toxicology:

- NNK increased by 9% [SE0004094]
- (b) (4) was added [SE0004094]
- The cigarette paper and the seam adhesive contained ingredients that were increased or newly added
- Multiple ingredients that were added or increased

All of the differences listed above have been demonstrated to not cause the new tobacco product to raise different questions of public health. The apparent increase in the NNK content in the smoke of the new tobacco product in SE0004094 is smaller than the analytical variability of the method used to collect the data. Therefore, the stated increase in NNK is not a valid concern. The amount (b) (4) added to the new tobacco product has been demonstrated by the applicant to raise no different questions of public health from a toxicological perspective. The applicant stated that flavors and other compounds were added to the tobacco in the new tobacco product that were not added to the predicate tobacco product. The applicant provided literature studies and data to demonstrate that the amount of additives and the likely pyrolysis products of those additives would not cause the new tobacco products to raise different questions of public health from a toxicological perspective. Finally, the applicant stated that there were increases or newly introduced additives in the cigarette paper and seam adhesive (b) (4) in the cigarette paper and (b) (4) in the seam adhesive) in the components of the new tobacco product. These additives are known to pyrolyze to formaldehyde and

isoprene in cigarette smoke. The applicant provided analytical data for the new and corresponding surrogate predicate products which demonstrated that there was no increase in the formaldehyde or isoprene content in the smoke of the new tobacco products. Therefore, the differences in characteristics between the new and corresponding surrogate predicate tobacco products do not cause the new tobacco products to raise different questions of public health related to toxicology.

4.4. SOCIAL SCIENCE

Social science reviews were completed by Cindy Tworek on January 17, 2013.

The final social science review concludes that the characteristics which may affect consumer perception and use are different for the new and corresponding predicate tobacco products, but the differences do not cause the new tobacco products to raise different questions of public health with respect to consumer perception and use.

The final social science 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 a social science 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 social science perspective.

The review also evaluated the health information summary and determined that it did not violate section 911(b)(2)(A)(i)(II) of the FD&C Act. Therefore, the final review did not identify a deficiency related to the health information summary.

5. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on April 5, 2018. The FONSI was supported by an environmental assessment prepared by FDA on April 5, 2018.

6. CONCLUSION AND RECOMMENDATION

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

- Decreased puff count
- The cigarette draw resistance, tobacco filler mass, cigarette paper base paper porosity, and filter pressure drop are lower (SE0004087 and SE0004173)
- Filter ventilation was added (SE0004087 and SE0004173)
- The filter is longer and the tipping paper is correspondingly longer (SE0004087 and SE0004173)
- The cigarette draw resistance is higher (SE0004094 only)
- The cigarette paper base paper porosity and the filter ventilation are lower (SE0004094 only)
- Lower total tobacco ((b) (4)
- Tobacco blend changes
- Menthol increase (SE0004088 and SE0004125)

- Increases in (b) (4) and (b) (4) in the filter tow and filter plug wrap, respectively (SE0004087 and SE0004173)
- NNK increased by 9% (SE0004094 only)
- (b) (4) increased (SE0004094 only)
- Increase in a variety of ingredients in the cigarette paper and the seam adhesive (b) (4) in the cigarette paper and (b) (4) in the seam adhesive)
- Increase in flavors and other compounds added to the tobacco ingredients

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. The differences in puff count, draw resistance, tobacco filler mass individually may lead to decreases in measured HPHCs. Therefore, the changes to puff count, draw resistance, tobacco filler mass do not cause the new tobacco product to raise different questions of public health. Changes in filter length (associated filter tipping paper increases) cigarette paper base paper porosity, and filter ventilation may result in changes in the HPHC yields for TNCOs and B[a]P. However, the analytical data shows no increases in TNCO and B[a]P yields for the new tobacco products when compared to the surrogate predicate tobacco products. A reduction in total tobacco content should result in lower HPHC yields and therefore, does not raise different questions of public health. The changes to the tobacco blends, (b) (4), flavors, and paper and adhesive additives may lead to changes in HPHC yields. None of the new tobacco products testing resulted in increases of HPHCs when compared to the surrogate predicate tobacco products, except for SE0004094. SE0004094 is reported to yield 9% higher NNK values in smoke testing under ISO and CI regimens. However, a 9% increase in NNK is within typical error in the analytical measurement of this very low concentration HPHC. The increases in (b) (4) in the filter tow and filter plug wrap are not combusted and the therefore, may only affect the ability of the filter to reduce the HPHC levels. The HPHC yields of the measured new tobacco products did not exceed those of the surrogate predicate tobacco products. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new tobacco products to raise different questions of public health.

The predicate tobacco products meet statutory requirements because 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 SE0004087, SE0004088, SE0004094, SE0004125, and SE0004173 as identified on the cover page of this review.