

**Technical Project Lead (TPL) Review: SE0015426 and SE0015427**

<b>SE0015426: Marlboro Red Label 100's Box</b>	
<b>Package Type</b>	Hard Pack
<b>Package Quantity</b>	20 Cigarettes
<b>Length</b>	98.5 mm
<b>Diameter<sup>1</sup></b>	7.89 mm
<b>Ventilation</b>	20%
<b>Characterizing Flavor</b>	None
<b>SE0015427: Benson &amp; Hedges 100's Box</b>	
<b>Package Type</b>	Hard Pack
<b>Package Quantity</b>	20 Cigarettes
<b>Length</b>	98 mm
<b>Diameter<sup>1</sup></b>	7.89 mm
<b>Ventilation</b>	26%
<b>Characterizing Flavor</b>	None
<b>Common Attributes of SE Reports</b>	
<b>Applicant</b>	Philip Morris USA Inc.
<b>Report Type</b>	Regular
<b>Product Category</b>	Cigarettes
<b>Product Sub-Category</b>	Combusted, Filtered
<b>Recommendation</b>	
Issue Substantially Equivalent (SE) orders.	

<sup>1</sup> The applicant submitted the circumference which allowed for a calculation of diameter.

**Technical Project Lead (TPL):**

Digitally signed by Jeannie H. Jeong-im -S  
Date: 2020.04.23 13:19:36 -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: 2020.04.23 14:18:15 -04'00'

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

## TABLE OF CONTENTS

<b>1. BACKGROUND .....</b>	<b>4</b>
1.1. PREDICATE TOBACCO PRODUCTS .....	4
1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW.....	4
1.3. SCOPE OF REVIEW .....	4
<b>2. REGULATORY REVIEW .....</b>	<b>5</b>
<b>3. COMPLIANCE REVIEW .....</b>	<b>5</b>
<b>4. SCIENTIFIC REVIEW .....</b>	<b>5</b>
4.1. CHEMISTRY.....	5
4.2. ENGINEERING .....	7
4.3. TOXICOLOGY.....	7
<b>5. ENVIRONMENTAL DECISION.....</b>	<b>8</b>
<b>6. CONCLUSION AND RECOMMENDATION .....</b>	<b>9</b>

**1. BACKGROUND**

**1.1. PREDICATE TOBACCO PRODUCTS**

The applicant submitted the following predicate tobacco products:

<b>SE0015426: Marlboro Red Label 100's Box</b>	
<b>Product Name</b>	Marlboro Red Label 100's Box
<b>Package Type</b>	Hard Pack
<b>Package Quantity</b>	20 Cigarettes
<b>Length</b>	98.5 mm
<b>Diameter</b>	7.89 mm
<b>Ventilation</b>	20%
<b>Characterizing Flavor</b>	None
<b>SE0015427: Benson &amp; Hedges 100's Box</b>	
<b>Product Name</b>	Benson & Hedges 100's Box
<b>Package Type</b>	Hard Pack
<b>Package Quantity</b>	20 Cigarettes
<b>Length</b>	98mm
<b>Diameter</b>	7.89 mm
<b>Ventilation</b>	26%
<b>Characterizing Flavor</b>	None

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

**1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW**

On September 5, 2019, FDA received two SE Reports from Altria Client Services LLC, on behalf of Philip Morris USA Inc. FDA issued Acknowledgment letters to the applicant on September 16, 2019. On November 20, 2019, FDA issued a Deficiency letter to the applicant. On January 29, 2020, FDA received an amendment (SE0015660) responding to the Deficiency letter.

<b>Product Name</b>	<b>SE Report</b>	<b>Amendment</b>
Marlboro Red Label 100's Box	SE0015426	SE0015660
Benson & Hedges 100's Box	SE0015427	

**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 Samuel Motto on September 16, 2019.

The reviews conclude that the SE Reports are administratively complete.

## **3. COMPLIANCE REVIEW**

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the applicant established that the predicate tobacco product in SE0015427 is a grandfathered product (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007). The OCE review dated October 6, 2019 concludes that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco product is grandfathered and, therefore is an eligible predicate tobacco product.

The predicate tobacco product in SE0015426 was determined to be substantially equivalent by FDA under SE0014849. Therefore, this product is an eligible predicate tobacco product.

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) (see section 910(a)(2)(A)(i)(II) of the FD&C Act). The OCE review dated April 3, 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**

Chemistry reviews were completed by Robert F. Gahl on October 24, 2019 and March 17, 2020.

The final 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:

SE0015426 and SE0015427:

- Tipping Paper Adhesive
  - Addition of (b) (4) mg/cigarette in SE0015426; (b) (4) mg/cigarette in SE0015427)

SE0015426:

- Cigarette Paper:
  - 14% decrease (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - 100% increase (b) (4) mg/cigarette) of (b) (4)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
- FSC Bands:
  - 587% increase (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)

SE0015427:

- Cigarette Seam Adhesive:
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - 3,233% increase (b) (4) mg/cigarette) of (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - 918% increase (b) (4) mg/cigarette) in (b) (4)
- Filter Seam Adhesive:
  - All ingredients changes less than (b) (4) mg/cigarette (b) (4)
  - Deletion of (b) (4) g/cigarette)

In both SE Reports, the applicant stated that the only changes to the new tobacco product compared to the corresponding predicate tobacco product was the addition of (b) (4) mg/cigarette and (b) (4) mg/cigarette of (b) (4) in SE0015426 and SE0015427, respectively, to the tipping adhesive and minor differences in the cigarette paper, cigarette seam adhesive, and filter seam adhesive. The tipping adhesive is mainly volatilized during manufacturing, and any residue is not expected to be burned, volatilized, or to be a potential source of thermal degradation resulting in the release of harmful and potential harmful constituents (HPHCs) and, therefore, the change of tipping adhesive ingredients in the new tobacco products does not cause the new tobacco products to raise different questions of

public health. However, in the cigarette paper in the new tobacco product in SE0015426, there is a 4% increase in (b) (4) content, a 587% increase in (b) (4), and an addition of (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. In the cigarette seam adhesive in the new tobacco product of SE0015427, there is an addition of (b) (4) and a 3,233% increase in (b) (4), which could affect the levels of acetaldehyde, acrolein, and benzene. The applicant provided complete data sets and method information for the mainstream smoke levels of these HPHCs under the ISO and CI regimen for the new and predicate tobacco products in SE0015426 and SE0015427. TOST<sup>2</sup> analysis comparing the levels of tar, nicotine, carbon monoxide, acetaldehyde, acrolein, acrylonitrile, ammonia, benzene, B[a]P, 1,3-butadiene crotonaldehyde, formaldehyde, isoprene, NNN, NNK, and toluene in the new tobacco products with the corresponding predicate tobacco products indicates that these levels are equivalent or lower in new tobacco products. 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 chemistry.

#### **4.2. ENGINEERING**

An engineering review was completed by Robert Meyer on October 21, 2019.

The engineering 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 an engineering 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 related to product engineering.

#### **4.3. TOXICOLOGY**

A toxicology review was completed by Prince Awuah on October 29, 2019.

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:

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<sup>2</sup> Two One-Sided T-test (TOST) is a statistical tool that calculates important analytical differences (IADs) using the Horwitz-Thompson equation.

- SE0015426 and SE0015427:
  - Tipping paper adhesive: (b) (4) (added)
- SE0015426:
  - Cigarette paper: (b) (4) (↑5.3%), (b) (4) (↑67%), (b) (4) (added), (b) (4) (↑233%), (b) (4) (added) and (b) (4) (added)
- SE0015427:
  - Cigarette Seam adhesive: (b) (4) (added), (b) (4) (↑323%), (b) (4) (added), and (b) (4) with 15 ingredients (added).
  - Filter Seam adhesive: (b) (4) with (b) (4) (↑4.2%), (b) (4) (↑12.5%), and (b) (4) (↑125%)

For both SE Reports, the applicant reported ingredient changes to the unburned portion of the new products including tipping adhesive and filter seam adhesive. These tipping components are in the unburned part of the cigarette and are not expected to be burned, volatilized, or to be a potential source of thermal degradation resulting in the release of HPHCs; therefore, inhalation exposure is unlikely. Potential dermal or oral exposures are also likely minimal, given that the ingredients of the tipping components are likely formulated into their respective matrices. The applicant also reported changes to ingredients in the combusted/burned region of the new products compare to the predicate products for both SE Reports, including cigarette paper and side seam adhesive, that may contribute to differences in HPHCs or have inherent toxicities if they should enter the mainstream smoke (MSS) unchanged by combustion. Ingredient changes that may be associated with the observed differences in HPHCs, assuming equal product use, include additions of (b) (4) in the cigarette paper, an addition of (b) (4) into the components of the side seam adhesive, and an addition of (b) (4) into the side seam adhesive. The HPHC comparisons in MSS using both ISO and CI regimens were provided by the applicant for both SE Reports and evaluated by Chemistry. The HPHC results provided by the applicant demonstrate that all HPHCs are analytically equivalent or decreased in the new products compared to the corresponding predicate products. Based on initial analysis of the HPHC data by Chemistry, the increases in cigarette paper ingredients (b) (4) do not result in analytical non-equivalent increases in any of the HPHCs submitted. As noted above, the side seam adhesive also contains the addition of a complex ingredient that includes (b) (4) a possible human carcinogen. The quantity of (b) (4) is small and any potential cancer risks, assuming any (b) (4) can in part enter the MSS unchanged by combustion, are expected to be offset by the decrease in other HPHCs, namely, formaldehyde. 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

Environmental reviews were completed by William Brenner on October 29, 2019 and March 11, 2020.



A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on March 19, 2020. The FONSI was supported by an environmental assessment prepared by FDA on March 19, 2020.

## 6. CONCLUSION AND RECOMMENDATION

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

SE0015426 and SE0015427:

- Tipping Paper Adhesive
  - Addition of (b) (4) mg/cigarette in SE0015426; (b) (4) mg/cigarette in SE0015427)

SE0015426:

- Cigarette Paper:
  - 14% decrease (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - 100% increase (b) (4) mg/cigarette) of (b) (4)
  - Deletion of (b) (4) mg/cigarette)
- FSC Bands:
  - 587% increase (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)

SE0015427:

- Cigarette Seam Adhesive:
  - 3,233% increase (b) (4) mg/cigarette) of (b) (4)
- Filter Seam Adhesive:
  - All ingredients changes less than (b) (4) mg/cigarette

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health (b) (4) is added to the tipping paper adhesive portions of both SE0015426 and SE0015427, but tipping paper adhesive is not a part of the cigarette that is combusted during normal cigarette use, and, therefore, is not expected to contribute to HPHC smoke yields. The modifications to the combusted components of SE0015426 include changes to the cigarette paper (such as decrease in (b) (4) addition of (b) (4) mg/cigarette of (b) (4) and 100% increase in (b) (4) and FSC band (such as 587% increase in (b) (4)). The modifications to the combusted components of SE0015427 include changes to the cigarette seam adhesive components (such as 3,233% increase in (b) (4) (b) (4)). Changes to the combusted components of the new products in SE0015426 and SE0015427 could lead to increases in MSS HPHC yields of tar, nicotine, carbon monoxide, acetaldehyde, acrolein, benzene, crotonaldehyde, formaldehyde, and B[a]P under both intense and non-intense smoking regimens. The applicant provided complete data sets in the 1st round of reviews and complete method information during the 2nd round of reviews for the MSS levels for

tar, nicotine, carbon monoxide, acetaldehyde, acrolein, acrylonitrile, ammonia, benzene, B[a]P, 1,3-butadiene crotonaldehyde, formaldehyde, isoprene, NNN, NNK, and toluene under the ISO and CI regimens for the new and predicate tobacco products in SE0015426 and SE0015427. TOST analysis comparing the levels of these HPHCs in the new tobacco products with the corresponding predicate tobacco products indicates that these HPHC levels are equivalent or lower in new tobacco products. As a result, the changes in the ingredients in the cigarette paper, cigarette seam adhesive and FSC band of the new tobacco products do not cause the new tobacco products to raise different questions of public health. The new tobacco product of SE0015427 also contains minor modifications to non-combusted component - Filter Seam Adhesive. All filter seam adhesive ingredients changes were either less than (b) (4) mg/cigarette or deletions. Filter Seam Adhesive is not a part of the cigarette that is combusted during normal cigarette use, and, therefore, is not expected to contribute to HPHC smoke yields. 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 product of SE0015427 meets statutory requirements because it was determined that they are grandfathered product (i.e., was commercially marketed in the United States other than exclusively in test markets as of February 15, 2007). The predicate tobacco product for SE0015426 was previously determined to be substantially equivalent by FDA under SE0014849.

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 SE0015426 was previously determined to be substantially equivalent by FDA under SE0014849. Comparison of the new tobacco product to the grandfathered product (Marlboro Medium 100's Box) reveals that the new tobacco product has the following differences in characteristics from Marlboro Medium 100's Box, the grandfathered tobacco product:

- Tipping Paper Adhesive:
  - Addition of (b) (4) mg/cigarette)
- Cigarette Paper:
  - 14% decrease (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - 100% increase (b) (4) mg/cigarette) of (b) (4)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)
- FSC Bands:
  - 587% increase (b) (4) mg/cigarette) in (b) (4)
  - Addition of (b) (4) mg/cigarette)
  - Addition of (b) (4) mg/cigarette)
  - Deletion of (b) (4) mg/cigarette)

- Base Tipping Paper:

- 211% increase in (b) (4)

The differences in characteristics listed above, other than the differences in cigarette paper, FSC bands, and adhesives, are the same differences in characteristics identified for the new and grandfathered tobacco products in SE0015426. Therefore, these differences do not cause the new tobacco product in SE0015426 to raise different questions of public health. Additionally, for the same reasons as discussed above, the differences in tipping paper adhesive, cigarette paper, FSC bands, and base tipping paper between the new tobacco product in SE0015426 and the grandfathered tobacco products does not cause the new tobacco product to raise different questions of public health. Therefore, whether comparing the new tobacco products in SE0015426 to the predicate of 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 SE0015426 and SE0015427, as identified on the cover page of this review.