



## Technical Project Lead (TPL) Review of SE Reports

<b>New Products Subject of this Review</b>	
Submission tracking numbers (STNs)	SE0016588-SE0016590, SE0016754, and SE0016755
<b>Common Attributes</b>	
Submission date	May 6, 2020 <sup>1</sup> and June 30, 2020 <sup>2</sup>
Receipt date	May 6, 2020 <sup>1</sup> and June 30, 2020 <sup>2</sup>
Applicant	John Middleton Co.
Product manufacturer	John Middleton Co.
Application type	Regular
Product category	Cigars
Product subcategory	Filtered and Unfiltered Sheet-Wrapped Cigars
<b>Cross-Referenced Submissions</b>	
All STNs	(b)(4) and (b)(4)
<b>Supporting FDA Memoranda Relied Upon in this Review</b>	
All STNs	None
<b>Recommendation</b>	
Issue Substantially Equivalent (SE) orders for the new tobacco products subject of this review.	

### Technical Project Lead (TPL):

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Date: 2022.01.18 11:26:15 -05'00'

Jeannie Jeong-Im, Ph.D.  
Chemistry Branch Chief, Division of Product Science  
Office of Science

### Signatory Decision:

Concur with TPL recommendation and basis of recommendation

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Date: 2022.01.18 12:48:41 -05'00'

Todd L. Cecil, Ph.D.  
Deputy Director  
Office of Science

<sup>1</sup> For SE0016588-SE0016590.

<sup>2</sup> For SE0016754-SE0016755.

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## 1. BACKGROUND

### 1.1. NEW AND PREDICATE PRODUCTS

The applicant submitted information for the new and predicate products listed in detail in the Appendix.

### 1.2. REGULATORY ACTIVITY

See Appendix for products and an amendment.

### 1.3. SCOPE OF REVIEW

This review captures all compliance, regulatory, and scientific reviews completed for the new products that are the subject of this review. Chemistry TPMF reviews for (b)(4) and (b)(4) were conducted for SE0016588-SE0016590, SE0016754, and SE0016755 which did not identify any deficiencies.

**Table 1. Disciplines reviewed**

Discipline	Cycle 1		Cycle 2	
	Reviewer(s)	Review Date	Reviewer(s)	Review Date
Regulatory	Maliha Choudhury	5/12/2020 <sup>3</sup>	N/A	N/A
	Travelle Mason	6/2/2020 <sup>4</sup>		
Chemistry	Salome Bhagan	12/7/2020 <sup>5</sup>	Ruth Ganunis	12/17/2021
Engineering	Robert Borthwick	12/2/2020	N/A	N/A
Toxicology	Shannon Dunn	12/7/2020 <sup>6</sup>	Maria Kaltcheva	1/5/2022
Microbiology	David Craft	12/1/2020	Kristy Huynh-Ngo	1/4/2022
Environmental Science	Gerome Burke	11/12/2020	Vyomesh Patel	1/6/2022

## 2. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed reviews to determine whether the applicant established that the predicate products are grandfathered products (i.e., were commercially marketed in the United States as of February 15, 2007). OCE reviews dated October 28, 2020, and October 30, 2020, conclude that the evidence submitted by the applicant is adequate to demonstrate that the predicate products are grandfathered and, therefore, are eligible predicate products.

OCE also completed reviews to determine whether the new 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). OCE reviews dated November 2, 2021 and January 12, 2022 conclude that the new tobacco products are in compliance with the FD&C Act.

<sup>3</sup> For SE0016588-SE0016590.

<sup>4</sup> For SE0016754-SE0016755.

<sup>5</sup> Addendum to the Chemistry Review were completed on December 9, 2020, to correct a typographical error in a deficiency and April 8, 2021 to revise which HPHCs are needed and update the deficiency.

<sup>6</sup> Addendum to the Toxicology Review was completed on December 15, 2020, to correct typographical errors in a deficiency.

### 3. SCIENTIFIC REVIEW

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

#### 3.1. CHEMISTRY

The final chemistry review concludes that the new products have different characteristics compared to the corresponding predicate products, but the differences do not cause the new products to raise different questions of public health from a chemistry perspective.

All SE Reports have a 2-34% decrease in (b)(4) with an addition (b)(4) mg/cigar of (b)(4) (b)(4) in SE0016589, 4-36% decrease in (b)(4) tobacco, 7-33% decrease in (b)(4) tobacco, and 9-12% decrease in (b)(4) in wrapper. Additionally, the new tobacco products in SE0016588 – SE0016590 have a 809 – 1295% increase in (b)(4) tobacco, 69 – 329% increase in (b)(4) (except SE0016589) and (b)(4) 3-28% decrease in tobacco rod density, and 43-56% increase in (b)(4). These differences between the new and corresponding predicate products may affect smoke HPHCs. For SE0016588, SE0016589, and SE0016590, the applicant provided tar, nicotine, carbon monoxide (TNCO) yields in mainstream smoke. TOST<sup>7</sup> analysis of the TNCO showed these were either equivalent or lower in the new products compared to the corresponding predicate products, with exception of nicotine in SE0016589. In response to deficiency on the 21% increase of nicotine, the applicant provided data supporting use of a 25% IAD in the TOST calculation for nicotine.<sup>8</sup> Therefore, the nicotine yields in the new and corresponding predicate products are analytically equivalent. For SE0016754 and SE0016755, the applicant provided arsenic, cadmium, nicotine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and N-nitrosornicotine (NNN) in the ground cigar, which were all equivalent or lower in the new tobacco products according to TOST analysis. The applicant also provided the following HPHCs in smoke in response to our deficiency on the differences between the new and corresponding predicate products for all SE Reports: acetaldehyde, acrolein, acrylonitrile, benzene, benzo[a]pyrene (B[a]P), 1,3-butadiene, carbon monoxide, crotonaldehyde, formaldehyde, isoprene, and toluene. For SE0016588 – SE0016590, the applicant also provided 4-aminobiphenyl, NNK, and NNN. Additionally, the applicant provided 1-aminonaphthalene, 2-aminonaphthalene, and ammonia for SE0016589. TOST analysis of these HPHC yields showed these were either equivalent or lower in the new products compared to the corresponding predicate products, with a few exceptions. Formaldehyde increases by 15-23% in SE0016588 and SE0016589 and there are increases in 1-aminonaphthalene (26%) and 4-aminobiphenyl (26%) in SE0016589. These increase are not equivalent by TOST analysis and have been deferred to toxicology for further evaluation. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new products to raise different questions of public health from a chemistry perspective.

<sup>7</sup> Two One-Sided T-test (TOST) is a statistical tool that calculates important analytical differences (IADs) using the Horwitz-Thompson equation.

<sup>8</sup> The applicant referenced SE0014879 where they had provided TNCO data for 107 tipped cigars manufactured by John Middleton Co. They used an IAD of 25% instead of 15% for nicotine to find the 22% increase in nicotine for SE0014879 was analytically equivalent. Using the same rationale for SE0016589, chemistry finds the 21% increase in nicotine to be analytically equivalent.

### 3.2. ENGINEERING

The engineering review concludes that the new products have different characteristics compared to the corresponding predicate products, but the differences do not cause the new products to raise different questions of public health from an engineering perspective.

For all SE Reports, there is a 6-33% decrease in tobacco filler mass and change in tobacco cut size. Also, SE0016588 – SE0016590 show a 13-28% decrease in tobacco rod density. A change in filler mass, tobacco cut size, and rod density may affect smoke constituent yields for tar, nicotine, and carbon monoxide. SE0016589 shows an increase in tobacco moisture, tipping paper, and filter length with changes in filter total denier, denier per filament, density, pressure drop due to changes in filter length. In addition to tar, nicotine, and carbon monoxide, these changes may also affect B[a]P yields in smoke. Therefore, these differences were deferred to chemistry for evaluation of any potential effects they may have on smoke chemistry including tar, nicotine, and carbon monoxide for all SE Reports and B[a]P for SE0016589. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new products to raise different questions of public health from an engineering perspective.

### 3.3. TOXICOLOGY

The final toxicology review concludes that the new products have different characteristics compared to the corresponding predicate products, but the differences do not cause the new products to raise different questions of public health from a toxicology perspective.

There is an increase in total tobacco and bright tobacco in SE0016588-SE0016590 and changes in sugar containing ingredients in all SE Reports. Also, there were some additions and higher-levels of non-tobacco ingredients in the filler, wrapper, seam adhesive of the new tobacco products, which may influence the some toxicity. The applicant provided mainstream smoke chemistry data for acetaldehyde, acrolein, acrylonitrile, benzene, benzo[a]pyrene, 1,3-butadiene, carbon monoxide, crotonaldehyde, formaldehyde, isoprene, and toluene for the new and corresponding predicate products. The applicant also provided in measurements for NNK, NNN, and 4-aminobiphenyl for the new and predicate products in SE0016588 - SE0016590, and measurements for 1-aminonaphthalene, 2-aminonaphthalene and ammonia for the new and predicate products in SE0016589. In SE0016590, SE0016754, and SE0016755, the measured mainstream smoke HPHC were either analytically equivalent or analytically non-equivalent and lower by TOST analysis. In SE0016588 and SE0016589, the analytically non-equivalent higher values in formaldehyde, 1-aminonaphthalene and/or 4-aminobiphenyl are likely offset by larger decreases in other carcinogens and toxicants. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new products to raise different questions of public health from a toxicology perspective.

### 3.4. MICROBIOLOGY

For SE0016754 and SE0016755, the final microbiology review did not identify any differences in characteristics between the new and corresponding predicate products that could cause the new products to raise different questions of public health from a microbiology perspective.

For SE0016588 – SE0016590, the final microbiology review concludes that the new products have different characteristics compared to the corresponding predicate products, but the differences do not cause the new products to raise different questions of public health from a microbiology perspective.

The new products in SE0016588 – SE0016590 have changes in (b)(4) and removal of (b)(4) which are both preservatives. Additionally, the new products have decreases in the content of (b)(4) (10-12%) in the seam adhesive, the humectants, (b)(4) ( $\leq 38\%$ ), (b)(4) ( $\leq 88\%$ ), and (b)(4) ( $\leq 71\%$ ), and increases in (b)(4) ( $\leq 56\%$ ). The applicant provided NNN and NNK content for the finished new and predicate products in the tobacco rod (filler, binder, and wrapper). NNN contents of the new products in SE0016588 and SE0016590 decreased 29%, and decreased by 34% in SE0016588. NNK contents of the new products in SE0016588 and SE0016590 decreased 50%, and decreased by 43% in SE0016589. Therefore, the differences in characteristics between the new and corresponding predicate products do not cause the new products to raise different questions of public health from a microbiology perspective.

#### 4. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by Luis Valerio, Ph.D. on January 6, 2022. The FONSI was supported by an environmental assessment prepared by FDA on January 6, 2022.

#### 5. CONCLUSION AND RECOMMENDATION

The new and the predicate products have the following characteristics:

- All SE Reports
  - Changes in tobacco cut size
  - 6-33% decrease in tobacco filler mass
    - 4–36% decrease in (b)(4) tobacco
    - 7–33% decrease in (b)(4) tobacco
    - 9–12% decrease in (b)(4) in wrapper
  - Deletion of (b)(4) (b)(4) mg/cigar) in binder and wrapper
  - Addition of (b)(4) (b)(4) mg/cigar) in binder and wrapper
- SE0016588, SE0016589, SE0016590
  - 13-28% decrease in tobacco rod density
  - 809-1295% increase in (b)(4)
  - 27-34% decrease in (b)(4)
  - 43-56% increase in (b)(4)
  - 10-12% decrease of (b)(4) in seam adhesive
  - 37-58% decrease in (b)(4)
- SE0016588
  - 15% increase in formaldehyde smoke yields
- SE0016589
  - 7% increase in tobacco moisture

- 5% decrease in cigar length
  - 23% increase in tipping paper length
  - Filter differences
    - 15% decrease in total denier
    - 6% increase in denier per filament
    - 9% decrease in filter density
    - 10% increase in pressure drop
    - 33% increase in length
  - 23 –64% increases in tip, filter seam, and filter anchor adhesives
  - 12% decrease in seam adhesive
  - removal of (b)(4) in the tip and seam adhesive.
  - 5 –38% increase tipping paper, filter tow, plasticizer, and plug wrap
  - increase of 6 –67% of brown inks and ink extenders
  - 21% increase in nicotine smoke yields
  - 23-26% increase in 1-aminonaphthalene, 4-aminobiphenyl, and formaldehyde smoke yields
- SE0016588, SE0016590, SE0016754, and SE0016755
    - 11% decrease in (b)(4) in binder
    - (b)(4) ng/cigar of (b)(4) deleted in the wrapper
    - 10% less seam adhesive and defoamer in the seam adhesive
  - SE0016588 and SE0016590
    - 11% increase of (b)(4)
  - SE0016588 and SE0016754
    - change from one plastic tip to another plastic tip
  - SE0016590 and SE0016755
    - change from plastic tips to wood tips

I concur with the conclusions of all the scientific reviews that the applicant has demonstrated that these differences in characteristics do not cause the new products to raise different questions of public health as described in Section 3.1-3.4 above. There are many differences between the new and corresponding predicate products such as a 6-33% decrease in tobacco filler mass in all SE Reports as well as decreases in tobacco rod density and (b)(4) and increases in (b)(4)

(b)(4) and (b)(4) in SE0016588 – SE0016590. In particular, there are many differences in SE0016589 including changes in design parameters (e.g., filter length, pressure drop, adhesives). The applicant provided TNCO for SE0016588 – SE0016590 and the following HPHCs in mainstream smoke: acetaldehyde, acrolein, acrylonitrile, benzene, benzo[a]pyrene (B[a]P), 1,3-butadiene, carbon monoxide, crotonaldehyde, formaldehyde, isoprene, and toluene for all SE Reports; 4-aminobiphenyl, NNK, and NNN for SE0016588 – SE0016590; and 1-aminonaphthalene, 2-aminonaphthalene, and ammonia for SE0016589. All of the yields new products were equivalent or lower than the corresponding predicate products according to TOST analysis except for a 15-23% increase in formaldehyde in SE0016588 and SE0016589 and a 26% increase in 1-aminonaphthalene and 4-aminobiphenyl for SE0016589. The analytically non-equivalent higher values in formaldehyde, 1-aminonaphthalene and/or 4-aminobiphenyl are likely offset by larger decreases in other carcinogens and toxicants. Therefore, the differences in characteristics between the new and

corresponding predicate products do not cause the new products to raise different questions of public health.

The predicate products meet statutory requirements because they were determined that they are grandfathered products (i.e., were commercially marketed in the United States as of February 15, 2007).

The new products are currently in compliance with the FD&C Act. I concur with these reviews and recommend that SE order letters be issued. FDA examined the environmental effects of finding these new products substantially equivalent and made a finding of no significant impact.



**6. APPENDICES<sup>9</sup>****Appendix A. New and predicate products**

<b>Common Attributes</b>		
Submission date	May 6, 2020 <sup>1</sup> and June 30, 2020 <sup>2</sup>	
Receipt date	May 6, 2020 <sup>1</sup> and June 30, 2020 <sup>2</sup>	
Applicant	John Middleton Co.	
Product manufacturer	John Middleton Co.	
Product category	Cigars	
Product subcategory	Unfiltered, Sheet-Wrapped <sup>10</sup> and Filtered, Sheet-Wrapped <sup>11</sup>	
<b>Attributes</b>	<b>New Product</b>	<b>Predicate Product</b>
<b>STN</b>	<b>SE0016588</b>	<b>GF1602193</b>
Product name	Black & Mild® Red Label	Prince Albert Soft Cherry Vanilla
Eligibility status	Not applicable	Grandfathered
Package type	Film <sup>12</sup>	Film <sup>12</sup>
Package quantity	1 cigar	1 cigar
Characterizing flavor	None	Cherry Vanilla
Length	126.9 mm	126.9 mm
Diameter	9.57 mm	9.62 mm
Tip	Plastic	Plastic
<b>STN</b>	<b>SE0016589</b>	<b>GF1602172</b>
Product name	Black & Mild® Red Label FT	Black & Mild FT
Eligibility status	Not applicable	Grandfathered
Package type	Film <sup>12</sup>	Film <sup>12</sup>
Package quantity	1 cigar	1 cigar
Characterizing flavor	None	None
Length	110 mm	110 mm
Diameter	8.9 mm	8.9 mm
Ventilation	None	None
<b>STN</b>	<b>SE0016590</b>	<b>GF1602193</b>
Product name	Black & Mild® Red Label Wood Tip	Prince Albert Soft Cherry Vanilla
Eligibility status	Not applicable	Grandfathered
Package type	Film <sup>12</sup>	Film <sup>12</sup>
Package quantity	1 cigar	1 cigar
Characterizing flavor	None	Cherry Vanilla
Length	126.9 mm	126.9 mm
Diameter	9.57 mm	9.62 mm
Tip	Wood	Plastic

<sup>9</sup> Brand/sub-brand or other commercial name used in commercial distribution.<sup>10</sup> SE0016588, SE0016590, SE0016754, and SE0016755.<sup>11</sup> SE0016589.<sup>12</sup> Cello is defined as clear film. The applicant considers cello and film to be synonymous when identifying cigar product packaging. Based on information provided in the SE Report, there is no change in the packaging between the new and predicate products, and for this submission, cello and film are synonymous.

<b>STN</b>	<b>SE0016754</b>	<b>GF1602166</b>
Product name	Black & Mild® Casino	Black & Mild
Eligibility status	Not applicable	Grandfathered
Package type	Film <sup>12</sup>	Film <sup>12</sup>
Package quantity	1 cigar	1 cigar
Characterizing flavor	None	None
Length	126.9 mm	126.9 mm
Diameter	9.57 mm	9.62 mm
Tip	Plastic	Plastic
<b>STN</b>	<b>SE0016755</b>	<b>GF1602166</b>
Product name	Black & Mild® Casino Wood Tip	Black & Mild
Eligibility status	Not applicable	Grandfathered
Package type	Film <sup>12</sup>	Film <sup>12</sup>
Package quantity	1 cigar	1 cigar
Characterizing flavor	None	None
Length	126.9 mm	126.9 mm
Diameter	9.57 mm	9.62 mm
Tip	Wood	Plastic

**Appendix B. Amendment**

<b>Submission Date</b>	<b>Receipt Date</b>	<b>Applications being amended</b>	<b>Reviewed</b>	<b>Brief Description</b>
July 13, 2021	July 13, 2021	All STNs	Yes	Response to April 20, 2021, Deficiency Letter