

**Technical Project Lead (TPL) Review:**

**SE0000116 - SE0000118, SE0006276 - SE0006284, SE0006288, and SE0006289**

<b>SE0000116: Natural American Spirit Perique Blend Rich Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	45%
Characterizing Flavor	None
<b>SE0000117: Natural American Spirit 100% US Grown Tobacco Full-Bodied Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	25%
Characterizing Flavor	None
<b>SE0000118: Natural American Spirit 100% US Grown Tobacco Mellow Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	40%
Characterizing Flavor	None
<b>SE0006276: Natural American Spirit Full-Bodied Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	20%
Characterizing Flavor	None

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

<b>SE0006277: Natural American Spirit Full-Bodied Taste SP</b>	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	20%
Characterizing Flavor	None
<b>SE0006278: Natural American Spirit Made with Organic Tobacco Full-Bodied Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	32%
Characterizing Flavor	None
<b>SE0006279: Natural American Spirit Made with Organic Tobacco Mellow Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	54%
Characterizing Flavor	None
<b>SE0006280: Natural American Spirit Mellow Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	35%
Characterizing Flavor	None
<b>SE0006281: Natural American Spirit Mellow Taste SP</b>	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	35%
Characterizing Flavor	None

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

<b>SE0006282: Natural American Spirit Menthol Full-Bodied Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	Menthol
<b>SE0006283: Natural American Spirit Menthol Mellow Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	32%
Characterizing Flavor	Menthol
<b>SE0006284: Natural American Spirit Non-filter</b>	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None
<b>SE0006288: Natural American Spirit Perique Blend Rich Robust Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	21%
Characterizing Flavor	None
<b>SE0006289: Natural American Spirit Smooth Mellow Taste</b>	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	60%
Characterizing Flavor	None

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

Common Attributes of SE Reports	
Applicant	Santa Fe Natural Tobacco Company, Inc.
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Combusted Filtered and Combusted Non-Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

**Technical Project Lead (TPL):**

Digitally signed by Kenneth Taylor -S  
Date: 2018.06.04 15:32:06 -04'00'

Kenneth M. Taylor, 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: 2018.06.05 13:36:23 -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:

<b>SE0000116: Natural American Spirit Perique Blend Rich Taste</b>	
Product Name	Predicate 1: Natural American Spirit Perique
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None
<b>SE0000117: Natural American Spirit 100% US Grown Tobacco Full-Bodied Taste</b>	
Product Name	Natural American Spirit Regular
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None
<b>SE0000118: Natural American Spirit 100% US Grown Tobacco Mellow Taste</b>	
Product Name	Natural American Spirit Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	35%
Characterizing Flavor	None
<b>SE0006276: Natural American Spirit Full-Bodied Taste</b>	
Product Name	Natural American Spirit Regular
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

<b>SE0006277: Natural American Spirit Full-Bodied Taste SP</b>	
Product Name	Natural American Spirit Regular
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None
<b>SE0006278: Natural American Spirit Made with Organic Tobacco Full-Bodied Taste</b>	
Product Name	Natural American Spirit Organic
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	29%
Characterizing Flavor	None
<b>SE0006279: Natural American Spirit Made with Organic Tobacco Mellow Taste</b>	
Product Name	Natural American Spirit Organic Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	49%
Characterizing Flavor	None
<b>SE0006280: Natural American Spirit Mellow Taste</b>	
Product Name	Natural American Spirit Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	35%
Characterizing Flavor	None

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

<b>SE0006281: Natural American Spirit Mellow Taste SP</b>	
Product Name	Natural American Spirit Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	35%
Characterizing Flavor	None
<b>SE0006282: Natural American Spirit Menthol Full-Bodied Taste</b>	
Product Name	Natural American Spirit Menthol
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	Menth ol
<b>SE0006283: Natural American Spirit Menthol Mellow Taste</b>	
Product Name	Natural American Spirit Menthol Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	28%
Characterizing Flavor	Menth ol
<b>SE0006284: Natural American Spirit Non-filter</b>	
Product Name	Natural American Spirit Non-filter
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	None
Characterizing Flavor	None



TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

<b>SE0006288: Natural American Spirit Perique Blend Rich Robust Taste</b>	
Product Name	Natural American Spirit Perique
Package Type	Box
Package Quantity	20 cigarettes
Length	84mm
Diameter	7.9mm
Ventilation	None
Characterizing Flavor	None
<b>SE0006289: Natural American Spirit Smooth Mellow Taste</b>	
Product Name	Natural American Spirit Ultra Lights
Package Type	Box
Package Quantity	20 cigarettes
Length	84mm
Diameter	7.9mm
Ventilation	56%
Characterizing Flavor	None

The predicate tobacco products are combusted filtered cigarettes and combusted non-filtered cigarettes manufactured by the applicant.

## 1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 15, 2011, FDA received the three SE Reports (SE0000116-SE0000118) from Santa Fe Natural Tobacco Company, Inc. FDA issued Acknowledgement letters on July 29, 2011. On March 22, 2011, FDA received 11 SE Reports (SE0006276-SE0006284 and SE0006288-SE0006289) from Santa Fe Natural Tobacco Company, Inc. FDA issued Acknowledgment letters on March 25, 2013. On June 15, 2012, FDA received a solicited amendment (SE0004576) from the applicant in response to FDA's June 10, 2012 request, seeking confirmation that the list of products and their corresponding tracking numbers accurately reflects the SE Reports submitted by the applicant to FDA. FDA issued Advice/Information Request (A/I) letters on June 18, 2012 for SE0000116-SE0000118. On June 29, 2012, FDA received amendments (SE0004646, SE0004647, and SE0004652) from the applicant requesting a 90-day extension to respond to FDA's A/I letters. FDA granted a 90-day extension on July 3, 2012. On September 10, 2012, FDA received amendments (SE0004910-SE0004912) in response the A/I letters.

On March 21, 2013, FDA received an amendment (SE0007894) requesting an extension to respond to the anticipated A/I letters for SE0006276-SE0006284 and SE0006288-SE0006289. FDA issued A/I letters on March 25, 2013, for SE0006276-SE0006284 and SE0006288-SE0006289. On March 27, April 1, April 5, April 9, and April 11, 2013, FDA conducted teleconferences to discuss the applicant's timeline and proposal to amend provisional SE Reports submitted by the applicant, including SE0006276-SE0006284 and SE0006288-SE0006289. On April 11, 2013, FDA received an amendment (SE0008212) containing the applicant's timeline and proposal to amend the SE Reports. FDA issued an Extension Response

letter on April 17, 2013, acknowledging receipt of the applicant's request for an extension to respond to the AI letter and encouraging the applicant to submit a complete response to all issues before the start of scientific review of the SE Reports.

On May 10, 2013, FDA issued a Public Health Impact (PHI) A/I letter to the applicant for the SE Reports, requesting full identification of the new and/or predicate tobacco products, full identification of a single predicate tobacco product, summary of differences in characteristics between the new and predicate tobacco products, and comparison of the tobacco blends in the new and predicate tobacco products, identifying the types and quantities of each tobacco. FDA received amendments in response to the PHI A/I letter on June 7, 2013, (SE0008936, SE0008933, SE0008937, SE0008901, SE0008934, and SE0008912), July 9, 2013 (SE0009211, SE0009213, SE0009214, SE0009216, SE0009217, SE0009218, and SE0009219), and on September 6, 2013 (SE0009739).

On December 9, 2016, FDA issued a Notification letter to inform the applicant that scientific review of the SE Reports would commence on January 23, 2017. On January 19, 2017, FDA received amendments (SE0013823-SE0013836) containing revised SE Reports. On February 13, 2017, FDA received a solicited amendment (SE0013901), in response to FDA's information request on February 7, 2017, for data needed concerning the predicate tobacco product evaluation. On February 22, 2017, FDA received an amendment (SE0013935) with corrections to previous amendments received on January 23, 2017 (SE0006277-SE0006278, SE0006281, and SE0006284).

FDA issued an A/I letter based on the scientific review of the SE Reports to the applicant on June 20, 2017. On August 18, 2017, FDA received an amendment (SE0014248) containing a response to the A/I letter. In this amendment, the applicant withdrew the second predicate product, Natural American Spirit Lights, for SE0000116. FDA issued a Preliminary Finding (Pfind) letter on December 7, 2017. On January 5, 2018, FDA received an amendment (SE0014462) containing a response to the Pfind letter.

Product Name	SE Report	Amendments
Natural American Spirit Perique Blend Rich Taste	SE0000116	SE0004576 SE0004646 SE0004910 SE0009211 SE0013831 SE0013901 SE0014248 SE0014462

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

Product Name	SE Report	Amendments
Natural American Spirit 100% US Grown Tobacco Full-Bodied Taste	SE0000117	SE0004576 SE0004647 SE0004911 SE0009213 SE0013832 SE0013901 SE0014248 SE0014462
Natural American Spirit 100% US Grown Tobacco Mellow Taste	SE0000118	SE0004576 SE0004652 SE0004912 SE0009214 SE0013828 SE0013901 SE0014248 SE0014462
Natural American Spirit Full-Bodied Taste	SE0006276	SE0007894 SE0008212 SE0008936 SE0013829 SE0013901 SE0014248 SE0014462
Natural American Spirit Full-Bodied Taste SP	SE0006277	SE0007894 SE0008212 SE0009216 SE0013836 SE0013901 SE0013935 SE0014248 SE0014462
Natural American Spirit Made with Organic Tobacco Full-Bodied Taste	SE0006278	SE0007894 SE0008212 SE0008933 SE0013834 SE0013901 SE0013935 SE0014248 SE0014462

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

Product Name	SE Report	Amendments
Natural American Spirit Made with Organic Tobacco Mellow Taste	SE0006279	SE0007894 SE0008212 SE0009217 SE0013833 SE0013901 SE0014248 SE0014462
Natural American Spirit Mellow Taste	SE0006280	SE0007894 SE0008212 SE0008937 SE0013830 SE0013901 SE0014248 SE0014462
Natural American Spirit Mellow Taste SP	SE0006281	SE0007894 SE0008212 SE0009218 SE0013824 SE0013901 SE0013935 SE0014248 SE0014462
Natural American Spirit Menthol Full-Bodied Taste	SE0006282	SE0007894 SE0008212 SE0008901 SE0013825 SE0013901 SE0014248 SE0014462
Natural American Spirit Menthol Mellow Taste	SE0006283	SE0007894 SE0008212 SE0008934 SE0013826 SE0013901 SE0014248 SE0014462

TPL Review for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289

Product Name	SE Report	Amendments
Natural American Spirit Non-filter	SE0006284	SE0007894 SE0008212 SE0009739 SE0013835 SE0013901 SE0013935 SE0014248 SE0014462
Natural American Spirit Perique Blend Rich Robust Taste	SE0006288	SE0007894 SE0008212 SE0009219 SE0013827 SE0013901 SE0014248 SE0014462
Natural American Spirit Smooth Mellow Taste	SE0006289	SE0007894 SE0008212 SE0008912 SE0013823 SE0013901 SE0014248 SE0014462

### 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 Marcella White on December 20, 2012, for SE0000116-SE0000118, and by Lea Lakes on March 12, 2018, for SE0006276- SE0006284 and SE0006288-SE0006289.

The final 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 February 21, 2017, 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. Since these are Provisional SE Reports, CWA/RRR is not required.

#### 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 Youbang Liu on May 16, 2017, and October 05, 2017.

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

- Differences in the tobacco blends for the new and corresponding predicate tobacco products:
  - 5% decrease in (b) (4) and 19% increase in (b) (4) for the new tobacco products in SE0000116 and SE0006288
  - 2% increase in (b) (4) and absence of (b) (4) for the new tobacco products in SE0000117 and SE0000118
  - 1% decrease in (b) (4) and 65% decrease in (b) (4) for the new tobacco products in SE0006278 and SE0006279
  - 4% decrease in (b) (4) and 15% increase in (b) (4) in the new tobacco products in SE0006276, SE0006277, SE0006280, SE0006281, SE0006282, SE0006283 and SE0006289
  - 1% decrease in (b) (4) and 17% increase in (b) (4) in the new tobacco product in SE0006284
- 3% less total tobacco compared to the corresponding predicate tobacco products, except for the new tobacco product reported in SE0006284, which has (b) (4) (0.1% difference) more total tobacco in the new tobacco product compared to the corresponding predicate tobacco product
- Addition of (b) (4) and removal of (b) (4) in the cigarette paper for the new products for all SE Reports
- Ingredient differences in non-combusted components of tipping paper, tipping paper adhesive and filter rod for all SE Reports

The decreases in total tobacco and specific tobacco types do not cause the new tobacco products to raise different questions of public health because these changes would not, by themselves, increase HPHC smoke yields. The ingredient differences in the tipping paper, tipping paper adhesive, and filter rods do not cause the new tobacco products to raise different questions of public health from a chemistry perspective because these are non-combusted components and, therefore, would not affect HPHC smoke yields. Because (b) (4) and (b) (4) account for about 0.2% of the paper weight, this ingredient change is not expected to cause the new tobacco products to raise different questions of public health. The only difference in product composition that could affect chemistry and that may cause the new tobacco products to raise different questions of public health are the significant increases in (b) (4) and

(b) (4). However, the applicant provided HPHC smoke data<sup>1</sup> under ISO and CI regimens for all new and corresponding predicate tobacco products. Among all of the tobacco products tested, SE0006288 was the only new product to have higher NNN and NNK smoke yields compared to the corresponding predicate product; under CI smoking regimen, NNN is 2% higher and NNK is 15% higher in the new product compared to the corresponding predicate product. However, the NNN and NNK smoke yields are within the expected 15% analytical variability, as discussed in scientific literature for routine testing of HPHCs in mainstream smoke. Thus, the higher (b) (4) in the new products do not cause the new products to raise different questions of public health. To address filter rod ingredient differences between the new and corresponding predicate products, the applicant provided TNCO data under ISO and CI (only for SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006280, SE0006281, SE0006284, SE0006288, and SE0006289) smoking regimens for the new and corresponding predicate tobacco products. Any increases in TNCO for the new tobacco products are within the published analytical variability of the methods and therefore do not cause concerns related to product chemistry. 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. ENGINEERING

Engineering reviews were completed by James Melchiors on May 25, 2017, and October 16, 2017.

The final engineering review concludes that the new tobacco products have different characteristics related to product engineering 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 for all SE Reports unless otherwise noted:

- Change in the FSC cigarette paper banding process
- Change in cigarette seam adhesive
- 2mm longer tobacco rod and 2mm longer filter rod
- Different tipping papers
- Different monogram inks
- Use of laser perforation to ventilate the tipping paper versus pre-perforated tipping paper
- Filter ventilation added to SE0000116, SE0000117, SE0006276, SE0006277, and SE0006288
- Increase in filter ventilation of 14%, 10%, 10%, 14%, and 7% for SE0000118, SE0006278, SE0006279, SE0006283, and SE0006289, respectively
- Filter rod designed with (b) (4) interspersed instead of in a hollow cavity for SE0006282 and SE0006283

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<sup>1</sup> NNN and NNK

The applicant provided targets, range limits, and test data for all relevant design parameters. The changes in the FSC banding process, cigarette seam adhesive, filter configuration, filter ventilation, and the location of (b) (4) do not cause the new tobacco products to raise different questions of public health from an engineering perspective. For the FSC banding process and cigarette seam adhesive, both the cigarette paper finished basis weight and the cigarette paper base weight decreased in the new tobacco products compared to the corresponding predicate tobacco products. This decrease in cigarette paper basis weight is less than 10% and represents less than 0.6% of the weight of the cigarettes. A decrease in the mass of a burned element of the tobacco product, such as cigarette paper, results in unchanged or decreased HPHC smoke yields. The increases in filter length, filter density, filter pressure drop, and total denier have been shown to decrease HPHC yields. These decreases in filter density and increases in filter denier per filament in some of the new filters are not a concern because they are offset, in part, by the overall improvements related to increases in filter length, density, pressure drop, and total denier. The new tobacco products in SE0006282 and SE0006283 also have different filter rod designs. The new tobacco products use a dual-segment filter comprised of a (b) (4) segment (mouth end) and a (b) (4) segment interspersed with (b) (4) (tobacco end). The corresponding predicate tobacco products use a tri-segment filter comprised of a hollow cavity section containing (b) (4), and (b) (4) segments on either end (mouth and tobacco ends). (b) (4) adsorbs polar gaseous compounds like ammonia. To address the difference in (b) (4) location, the applicant provides a summary of expected (b) (4) values in the new and corresponding predicate products. For SE0006282 and SE0006283, the expected (b) (4) values (mg per segment) are approximately 85% and 45% lower in the new products compared to the corresponding predicate products, respectively. Additionally, none of the new tobacco products produced statistically relevant increases in HPHC smoke yields. 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 an engineering perspective.

### 4.3. MICROBIOLOGY

A microbiology review for SE0000116 and SE0006288 was completed by David Craft on May 15, 2017. No microbiology information was found in the other SE Reports, so the microbiology review did not evaluate those SE Reports.

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

- 19% increase in (b) (4)

Microbiology only reviewed SE0000116 and SE0006288 since the new tobacco products contain (b) (4). The (b) (4) leaf content of the new tobacco products does not exceed 10% of the total tobacco blend. The applicant provided target moisture content of the tobacco blend for the new and corresponding predicate tobacco products, which was (b) (4). Tobacco blend moisture content of 15% or lower is insufficient to



support fungal growth and comprehensive data to support bacterial growth at moisture contents of 15% have not been substantiated. 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 microbiology perspective.

#### 4.4. TOXICOLOGY

Toxicology reviews were completed by Shaji Theodore on May 26, 2017, October 02, 2017, and February 15, 2018.

The final 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:

- SE0000116 – SE0000118, SE0006276, SE0006277, SE0006280 – SE0006284, SE0006288, and SE0006289: (b) (4) was added to the seam adhesive of the new tobacco products
- SE0006278 and SE0006279: (b) (4) was added to the seam adhesive of the new tobacco products
- SE0006282: acrolein was increased in the CI mainstream smoke by 7%
- SE0006289: benzene was increased in the CI mainstream smoke by 1.5%
- Toluene was increased in the CI mainstream smoke by 7.6% in SE0006289 and by 2% in SE0006284

The new tobacco products in SE0000116 – SE0000118, SE0006276, SE0006277, SE0006280 – SE0006284, SE0006288, and SE0006289 contain (b) (4), which is a (b) (4) used in the seam adhesives. Upon combustion, (b) (4) could potentially yield the respiratory toxicant vinyl acetate, an HPHC. The applicant provided HPHC data, which indicated that the levels of HPHCs in the new tobacco products in the above SE Reports were comparable to or lower than those in the corresponding predicate tobacco products. The applicant measured (b) (4) in the tobacco rod and in mainstream smoke and demonstrated that vinyl acetate levels in the tobacco rod and mainstream smoke of the new tobacco products were lower than those in the corresponding predicate tobacco products. The applicant also showed that the calculated daily exposure to (b) (4) from cigarette smoke of the new tobacco products was 12.5 to 20-fold lower than the reference concentration for (b) (4). Therefore, the inclusion of (b) (4) does not cause the new tobacco products to yield a higher level of (b) (4) when compared to the corresponding predicate tobacco products and does not cause the new tobacco products to raise different questions of public health from a toxicology perspective.

The new tobacco products in SE0006278 and SE0006279 contain (b) (4) with a potential for respiratory sensitization and irritation. Although the levels of (b) (4) were higher in the new tobacco products compared to the corresponding predicate tobacco products, the levels of NO<sub>x</sub> and SO<sub>2</sub>, the products of thermal decomposition of (b) (4), in the mainstream smoke of the new tobacco

products were lower when compared to those of the corresponding predicate tobacco products. Furthermore, the levels of SO<sub>2</sub> in the mainstream smoke of the new tobacco products were lower in comparison to SO<sub>2</sub> levels in ambient air. Therefore, the addition of (b) (4) to the seam adhesives in the new tobacco products in SE0006278 and SE0006279 does not cause the new tobacco products to raise different questions of public health from a toxicology perspective.

The new tobacco products in SE0006282, SE0006284, and SE0006289 had respective increased CI smoke yields of benzene (1.5%) and toluene (7.6%), toluene (2.0%), and acrolein (7.2%). A separate statistical equivalence test was performed to determine whether the mean HPHC values between the new and predicate tobacco products were analytically equivalent. The Important Analytical Difference (IAD) was set at 20% for toluene and benzene, and 15% for acrolein. Upper and lower equivalence margins were calculated using the IAD. The mean range was calculated for the HPHCs and was found to be within the upper and lower equivalence margin, indicating that the mean values of the new tobacco products were equivalent to those of the corresponding predicate tobacco products and the HPHC increase is within the range of analytical variability. Therefore, the observed increases in toluene, benzene, and acrolein do not cause an increase in the toxicity of the new tobacco products and do not cause the new tobacco products to raise different questions of public health from a toxicology 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 toxicology perspective.

## 5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(a), issuance of SE orders under section 910(a) of the FD&C Act for these provisional SE Reports (SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289) is categorically excluded and, therefore, normally does not require the preparation of an environmental assessment (EA) or an environmental impact statement. FDA has considered whether there are extraordinary circumstances that would require the preparation of an EA and has determined that none exist.

## 6. CONCLUSION AND RECOMMENDATION

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

- Differences in the tobacco blends for the new and corresponding predicate tobacco products include:
  - SE0000116 and SE0006288: decrease in (b) (4) and 19% increase in (b) (4) for the new tobacco products
  - SE0000117 and SE0000118: 2% increase in (b) (4) and absence of (b) (4) for the new tobacco products
  - SE0006278 and SE0006279: 1% decrease in (b) (4) and 65% decrease in (b) (4) for the new tobacco products

- SE0006276, SE0006277, SE0006280, SE0006281, SE0006282, SE0006283 and SE0006289: 4% decrease in (b) (4) and 15% increase in (b) (4) in the new tobacco products
- SE0006284: 1% decrease in (b) (4) and 17% increase in (b) (4) in the new tobacco product
- 3% less total tobacco compared to the corresponding predicate tobacco products, except for the new tobacco product reported in SE0006284, which has (b) (4) more total tobacco in the new tobacco product compared to the corresponding predicate tobacco product
- Addition of (b) (4) and removal of (b) (4) in the cigarette paper for the new products for all SE reports
- Ingredient differences in the noncombusted components of tipping paper, tipping paper adhesive and filter rod for the new tobacco products.
- Change in the FSC cigarette paper banding process
- Change in cigarette seam adhesive
- 2mm longer tobacco rod and 2mm longer filter rod
- Different tipping papers
- Different monogram inks
- Use of laser perforation to ventilate the tipping paper versus pre-perforated tipping paper
- Filter ventilation added to SE0000116, SE0000117, SE0006276, SE0006277, and SE0006288
- Increase in filter ventilation of 14%, 10%, 10%, 14%, and 7% for SE0000118, SE0006278, SE0006279, SE0006283, and SE0006289, respectively
- Filter designed with (b) (4) interspersed instead of in a cavity for SE0006282 and SE0006283
- SE0000116 – SE0000118, SE0006276, SE0006277, SE0006280 – SE0006284, SE0006288, and SE0006289: (b) (4) was added to the seam adhesive of the new tobacco products
- SE0006278 and SE0006279: (b) (4) was added to the seam adhesive of the new tobacco products
- SE0006282: acrolein was increased in the CI mainstream smoke by 7%
- SE0006289: benzene was increased in the CI mainstream smoke by 1.5%
- Toluene was increased in the CI mainstream smoke by 7.6% in SE0006289 and by 2% in SE0006284

The applicant has demonstrated that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. Test data for HPHCs under ISO and CI smoking regimens support that the differences in tobacco and nontobacco ingredients or other design parameters (filter ventilation) between the new and corresponding predicate products do not cause the new tobacco products to raise different questions of public health. A microbiology review was performed for SE0000116 and SE0006288 since the new tobacco products contain (b) (4) which is fermented. The target moisture content is less than 15% and therefore insufficient to support microbial growth. Thus, the use of (b) (4) in the new tobacco products in SE0000116 and SE0006288 is not a concern. The toxicology review concludes that the inclusion of (b) (4) (SE0006278 and SE0006279) does not cause the new tobacco products to raise different questions of public health. The toxicology review also

concludes that the increases in intense smoke yields of benzene and toluene (SE0006282), toluene (SE0006284), and acrolein (SE0006289) are not statistically significant. 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 it was determined that they are grandfathered products (i.e., were commercially marketed in the United States other than exclusively in test markets as of February 15, 2007).

In addition, all of the scientific reviews conclude that the differences between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health. I concur with the discipline reviews and recommend that SE order letters be issued.

Because the proposed action is issuing SE orders for these provisional SE Reports, it is a class of action that is categorically excluded under 21 CFR 25.35(a). FDA has considered whether there are extraordinary circumstances that would require the preparation of an environmental assessment and has determined that none exist. Therefore, the proposed action does not require preparation of an environmental assessment or an environmental impact statement.

SE order letters should be issued for the new tobacco products in SE0000116, SE0000117, SE0000118, SE0006276, SE0006277, SE0006278, SE0006279, SE0006280, SE0006281, SE0006282, SE0006283, SE0006284, SE0006288, and SE0006289, as identified on the cover page of this review.