FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review: SE0013372 - SE0013375 and SE0013384 - SE0013387

SE0013372: Native Full Flavor 100's Hard Pack (2016)	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013373: Native Full Flavor 100's Soft (2016)	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013374: Native Full Flavor King Hard Pack (2016)	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013375: Native Full Flavor King Soft (2016)	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013384: Native Menthol 100's Hard Pack (2016)	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol

SE0013385: Native Menthol 100's Soft (2016)	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
SE0013386: Native Menthol King Hard Pack (2016)	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
SE0013387: Native Menthol King Soft (2016)	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
Common Attributes of SE Reports	
Applicant	Susan Jesmer d/b/a Native Trading Associates
Report Type	Regular
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

Todd L. Cecil -S
Digitally signed by Todd L. Cecil -S
Date: 2018.05.03 15:32:21 -04'00'

Todd L. 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: 2018.05.03 15:49:31 -04'00'

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

TABLE OF CONTENTS

1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0013372: Native Full Flavor 100's Hard Pack (2016)	
Product Name	Native Full Flavor 100's Hard Pack
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013373: Native Full Flavor 100's Soft (2016)	
Product Name	Native Full Flavor 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013374: Native Full Flavor King Hard Pack (2016)	
Product Name	Native Full Flavor King Hard Pack
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None
SE0013375: Native Full Flavor King Soft (2016)	
Product Name	Native Full Flavor King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	None

SE0013384: Native Menthol 100's Hard Pack (2016)	
Product Name	Native Menthol 100's Hard Pack
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
SE0013385: Native Menthol 100's Soft (2016)	
Product Name	Native Menthol 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	100 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
SE0013386: Native Menthol King Hard Pack (2016)	
Product Name	Native Menthol King Hard Pack
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol
SE0013387: Native Menthol King Soft (2016)	
Product Name	Native Menthol King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.9 mm
Ventilation	4%
Characterizing Flavor	Menthol

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On May 23, 2016, the applicant submitted the regular SE Reports. On August 8, 2016, FDA requested clarification via email regarding the relationship of the Alternate New tobacco products containing (b) (4) [redacted], referenced in the applications, with the new

tobacco products and if new reports should be created to reflect the Alternate New tobacco products. On August 12, 2016, the applicant submitted an amendment (SE0013580) for all SE Reports stating they did not want the Alternate New tobacco products containing (b) (4) [redacted] to be considered new tobacco products, and FDA should proceed with review of the new and predicate tobacco products containing (b) (4) [redacted]. FDA issued an Advice/Information (A/I) Request letter for all SE Reports on August 12, 2016. On October 6, 2016, the applicant submitted an amendment (SE0013723) in response to the A/I Request letter for all SE Reports. A Preliminary Finding letter was issued for all SE Reports on April 14, 2017. On May 12, 2017, the applicant responded to the Preliminary Finding letter (SE0014084). A Preliminary Finding letter identifying environmental assessment deficiencies for all SE Reports was issued on August 10, 2017. On September 5, 2017, the applicant submitted an amendment in response to the Preliminary Finding letter (SE0014307). On December 5, 2017, FDA issued an A/I Request letter for all SE Reports, to inform the applicant that it had not paid all of its user fees assessed under section 919 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act). FDA explained that, because the applicant was not current on its user fee payments, its tobacco products were not in compliance with the requirements of the FD&C Act and FDA could not issue SE marketing orders under section 910(a)(2)(A)(i) of the FD&C Act for its new tobacco products. FDA requested the applicant inform the Agency as to the date it intended to make full payment of all user fees assessed. On February 2, 2018, FDA received an amendment (SE0014502) containing the applicant's plan for making full payment of all user fees assessed. On March 16, 2018, FDA received an amendment (SE0014664) from the applicant, modifying its plan. The applicant made full payment of all user fees assessed on April 19, 2018.

Product Name	SE Report	Amendments
Native Full Flavor 100's Hard Pack (2016)	SE0013372	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Full Flavor 100's Soft (2016)	SE0013373	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Full Flavor King Hard Pack (2016)	SE0013374	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664

Product Name	SE Report	Amendments
Native Full Flavor King Soft (2016)	SE0013375	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Menthol 100's Hard Pack (2016)	SE0013384	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Menthol 100's Soft (2016)	SE0013385	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Menthol King Hard Pack (2016)	SE0013386	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664
Native Menthol King Soft (2016)	SE0013387	SE0013580 SE0013723 SE0014084 SE0014307 SE0014502 SE0014664

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 Sarah Webster on May 31, 2016. The reviews conclude that the SE Reports are administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed reviews for all SE Reports 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). On June 30, 2016, OCE reviews for all SE Reports concluded 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.

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the new tobacco products are in compliance with the requirements of the FD&C Act (see section 910(a)(2)(A)(i)(II) of the FD&C Act). The OCE review dated December 5, 2017, concludes that the new tobacco products are not in compliance with section 919 the FD&C Act. The OCE review dated April 19, 2018, concludes that the new tobacco products are now 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 Shixia Feng on August 4, 2016, Karina Zuck on December 1, 2016, and Lida Oum on June 23, 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. The reviews identified the following differences:

- Addition of standard compliant (FSC) cigarette paper in place of non-FSC cigarette paper
- Addition of (b) (4) of (b) (4) per cigarette
- Increase (13%) of (b) (4) in the cigarette paper
- Increase (39% to 41%) of (b) (4) in the plug wrap

The new tobacco products include FSC cigarette paper containing (b) (4) and (b) (4) that are not present in the cigarette paper for the predicate tobacco products. This difference in cigarette paper may cause the new tobacco products to produce different types and quantities of HPHCs such as formaldehyde, acetaldehyde, and benzene when compared to the corresponding predicate tobacco products. The applicant provided data obtained from the new and corresponding predicate tobacco products using a valid analytical method and the results demonstrated no statistically significant differences in HPHC values. Additionally, the new tobacco products contain increases in (b) (4) levels to cigarette papers that may lead to increases in carbon monoxide production. The applicant provided carbon monoxide yields for the new and corresponding predicate tobacco products that are statistically different, but within the error of the measurement. The increase in (b) (4) in the plug wrap will not affect filter ventilation or smoke yields because the plug wraps used in the new and predicate products are non-porous plug wraps. Moreover, higher (b) (4) quantities in the plug wrap paper could reduce filter ventilation and produce higher levels of benzene and acetaldehyde. However, there is no statistically significant difference of acetaldehyde or benzene in the new products compared to the corresponding predicate 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 from a chemistry perspective.

4.2. ENGINEERING

Engineering reviews were completed by Aarthi Arab on July 29, 2016, December 7, 2016, and June 30, 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 and that the SE Reports lack adequate evidence to demonstrate that the differences do not cause the new tobacco products to raise different questions of public health. The review identifies the following deficiencies that have *not* been adequately resolved:

1. In the SE Reports listed below, individual data points fall outside the previously submitted range limits and acceptance criteria for certain new and predicate tobacco products. Additionally, you do not provide any information on how you handle products and subcomponents that fall outside of the range limits. Test data that falls outside of the range limits indicate that the target specifications and range limits may not adequately characterize the end products. Provide justification for these discrepancies and clarify how products that do not meet target specifications and range limits are handled.

    a. Tobacco moisture (all new and predicate tobacco products except the predicate tobacco products in SE0013384-SE0013385):

    You submitted several papers to justify that although data points fall outside of the range limits, they do not cause the new tobacco product to raise different questions of public health. However, the papers that you provided only look at moisture changes of 5% and not at the smaller differences in tobacco moisture that are seen outside of the range limits. At 5%, the papers find that there are sufficient differences observed in the TNCO yields. You did not provide scientific evidence that tobacco moisture differences of less than 5% outside of the range limits do not raise different questions of public health.

    b. Cigarette paper base paper porosity (only predicate tobacco products)

    You submitted several different range limits for cigarette base paper porosity – those used by the supplier (based on target specifications) and those used by you, Native Trading Associates (based on average values). It is unclear which range limits are used as acceptance criteria to accept or reject the base paper or if there is a process to identify and reject cigarette base paper based on base paper porosity. Test data that falls outside of the range limits indicate that the target specifications and range limits may not adequately characterize the end products. Provide a single acceptance criteria used to evaluate the cigarette base paper porosity test data to

demonstrate that the end products are well characterized by the target specifications.

c. Filler mass (predicate tobacco products in SE0013372 and SE0013373, and new tobacco products in SE0013374 and SE0013375[1])

You submitted individual data points from the test data for filler mass but it falls outside the previously submitted range limits and acceptance criteria for the above new and predicate tobacco products. You do not provide any information on how you handle products and subcomponents that fall outside of the range limits.

2. In SE0013372-SE0013373 and SE0013384-SE0013385, there are significant decreases in open draw resistance that are not accompanied or explained by differences in other design parameters. Provide scientific rationale and published or unpublished evidence to justify why this decrease in open draw resistance does not cause the new tobacco products in SE0013372-SE0013373 and SE0013384-SE0013385 to raise different questions of public health.

Therefore, the review concludes that the applicant did not demonstrate that 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.

Although the engineering review found that the above deficiencies have not been resolved, I, the Technical Project Lead, found that these deficiencies are adequately addressed. As discussed above, the engineering review identified deficiencies related to the following two issues: three sets of measured values include test data that falls outside the applicant's upper and lower range limit acceptance criteria (tobacco moisture, cigarette paper base paper porosity, and tobacco filler mass); and the new tobacco products (SE0013372, SE0013373, SE0013384, and SE0013385 only) have a decreased open draw resistance, relative to the corresponding predicate tobacco products. The applicant provided measured cigarette paper base paper porosity, tobacco moisture and tobacco filler mass values that are outside of their stated acceptance criteria for the associated parameters. The applicant did not provide a rationale for exceeding the limits, the effects of exceeding the limits, or the process for addressing out-of-specification test data. The test data including the range limits provided by the applicant (not by the supplier) for cigarette paper base paper porosity of the predicate tobacco products included 3 of 10 measurements outside of the claimed acceptance criteria; each of those 3 measurements is less than 5% and averaging 2.7% outside of the acceptance criteria. The applicant stated that the tobacco moisture measurement excursions occurred in 5 of the 6 measurements for the new tobacco products (each of the out-of-specification measurement range from 1.5-5% outside the range) and 1 of 4 measurements for the predicate tobacco products (the out-of-specification measurement is 1% outside the range). The applicant provided measurements of the tobacco filler mass in the predicate tobacco product that exceed the acceptance range limits in 2 of the 20 measurements for SE0013372 and SE0013373. The applicant also provided measurements of the tobacco filler mass in the new tobacco products that exceed the acceptance range limits in 1 of the 20 measurements for SE0013374,

[1] Although not listed in the deficiency, this also applies to the new tobacco products in SE0013386 and SE0013387.

SE0013375, SE0013386 and SE0013387. Each of the tobacco filler mass measurements is 0.5-2% higher than the stated acceptance range limit. The applicant also provided measured open cigarette draw resistance values for the new and predicate tobacco products. The new tobacco products (SE0013372, SE0013373, SE0013384, and SE0013385 only) were found to have a lower open cigarette draw resistance, relative to the corresponding predicate tobacco products, than could be explained by the filter ventilation.[2] The applicant provided no rationale to explain the measured findings.

To address the tobacco moisture values that were outside the stated acceptance range limits, the applicant provided published literature. The literature shows that a 5% increase or more in tobacco moisture leads to an increase in TNCO yields, but the excursions beyond the acceptance range limits are each less than 5% and the literature does not describe how smaller differences in these products may affect TNCO yields. The average tobacco moisture values for the new and corresponding predicate tobacco products are the same. Generally, differences in tobacco moisture may lead to changes in the puff count, which will affect TNCO yields in machine testing. However, for these SE Reports, the target values for tobacco moisture for the new and corresponding predicate tobacco products are the same. Moreover, the applicant provided the measured TNCO values that could be influenced by differences in tobacco moisture, and these TNCO values were decreased in the new tobacco products relative to the corresponding predicate tobacco products. As a result, I conclude that the data outside the acceptance range limits for tobacco moisture does not cause the new tobacco products to raise different questions of public health.

With regards to the cigarette paper base paper porosity, the applicant submitted test data that fell outside its stated acceptance range limits (not the supplier's acceptance range), indicating that the predicate tobacco products may have higher TNCO values than would be expected for products produced within the acceptance ranges.[3] Nonetheless, the measured TNCO values all showed a decrease in the new tobacco products relative to the corresponding predicate tobacco products. Thus, I conclude that the data outside the acceptance range limits for cigarette paper base paper porosity does not cause the new tobacco products to raise different questions of public health.

With regards to the tobacco filler mass, I find that, despite individual data points for tobacco filler mass falling outside the acceptance range limits, the average filler mass values for the new and corresponding predicate tobacco products are within acceptance range limits. Generally, a change in tobacco filler mass may affect specific HPHCs or classes of HPHCs (carbonyls, PAHs, VOCs, etc.). For these SE Reports, however, the tobacco filler mass target values for the new and corresponding predicate tobacco products are the same. Moreover, the applicant provided measured smoke yields of all the HPHCs of concern that could be influenced by differences in tobacco filler mass (based upon the specific tobacco blend, these were formaldehyde, acetaldehyde or benzene); and these HPHC yields were equivalent or lower in the new tobacco products relative to corresponding predicate tobacco products. The result of out-of-

[2] The new and predicate tobacco products in SE0013372-SE0013373 and SE0013384-SE0013385 have the same ventilation: 4%.
[3] The applicant provided two different acceptance range limits for cigarette paper base paper porosity, one from the applicant and one from the suppliers' COA. Without further clarification, it is presumed that the acceptance range limits provided by the applicant describe the acceptance ranges of the materials that may be used in the finished tobacco product and that the COA acceptance range limits describe the specification of the cigarette paper base paper supplier. Therefore, the design parameters acceptance range limits provided by the applicant were used for the comparison of the new and predicate tobacco products.

specification measurements would be a higher variability in the results of the TNCO measurements of the new and predicate tobacco products, which is seen in the chemistry data. However, the standard deviations of the tobacco product filler mass values for the predicate tobacco products in SE0013372 and SE0013373 and the new tobacco products in SE0013374, SE0013375, SE0013386 and SE0013387 are within acceptable ranges and the new tobacco products yield approximately the same or lower amounts of tar and nicotine than the corresponding predicate tobacco products. Therefore, I conclude that the data outside the acceptance range limits for tobacco filler mass does not cause the new tobacco products to raise different questions of public health.

Regarding the decrease in open draw resistance, the applicant submitted data showing that the new tobacco products (SE0013372, SE0013373, SE0013384, and SE0013385) have a lower open cigarette draw resistance, relative to the corresponding predicate tobacco products, than could be explained by filter ventilation, and did not provide a rationale to explain why this difference does not cause the new tobacco products to raise different questions of public health. A decrease in open draw resistance may lead to a decrease in the resistance needed to inhale smoke and an increase in inhaled smoke constituent yields. Nevertheless, the applicant submitted evidence demonstrating that the new tobacco products contain similar or lower HPHCs yields under ISO and CI regimens when compared to the predicate tobacco products and that the variability of those measurements is within the expected variability of the analytical methods. As such, I conclude that the difference in open draw resistance between the new and corresponding predicate tobacco products does not cause the new tobacco products to raise different questions of public health.

For the reasons stated above and based on all of the information provided by the applicant, including but not limited to HPHC and TNCO data, I find that the deficiencies identified in the engineering review have been adequately resolved and that the applicant has demonstrated that the differences related to product engineering between the new and corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health.

4.3. TOXICOLOGY

Toxicology reviews were completed by Mayo Wright on August 4, 2016, January 17, 2017, and June 28, 2017.[4]

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:

- Addition of (b) (4) and (b) (4)
- Increase in (b) (4)

[4] The January 17, 2017, review found that the new tobacco products have different characteristics compared to the corresponding predicate tobacco products, but that the SE Reports demonstrate that these differences do not raise different questions of public health from a toxicology perspective. The June 28, 2017, review listed the SE Reports, but did not further evaluate them.

The SE Reports indicate that the cigarette paper in the new tobacco products contains (b) (4) and (b) (4) while the corresponding predicate tobacco products do not and that the (b) (4) levels are increased in the new tobacco products from the corresponding predicate tobacco products. (b) (4) and (b) (4) can produce HPHCs, including formaldehyde, acetaldehyde, and benzene, upon pyrolysis. The applicant provided chemical analyses of the smoke obtained from the new and predicate tobacco products which did not indicate a statistically significant increase in the formaldehyde, acetaldehyde, or benzene levels. 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

A finding of no significant impact (FONSI) was signed by Kimberly Benson, Ph.D. on October 20, 2017. The FONSI was supported by an environmental assessment prepared by FDA on October 20, 2017.

6. CONCLUSION AND RECOMMENDATION

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

- Addition of fire standard compliant (FSC) cigarette paper in place of non-FSC cigarette paper
- Increase in (b) (4) in the cigarette paper and plug wrap
- Decrease in open draw resistance (SE0013372, SE0013373, SE0013384, and SE0013385)
- Addition of (b) (4) and (b) (4)
- Increase in (b) (4)

All of the reviews *except* engineering conclude that the differences in characteristics do not cause the new tobacco products to raise different questions of public health. I concur with all of the reviews *except* engineering. The engineering review identified deficiencies related to the new tobacco products (SE0013372, SE0013373, SE0013384, and SE0013385 only) which have a decrease in open draw resistance, relative to the corresponding predicate tobacco products. I find that the applicant provided adequate scientific evidence and rationale to resolve these deficiencies. The applicant provided measured smoke yields of all the HPHCs of concern that could be influenced by differences in open draw resistance in the new tobacco products, and these values were equivalent or lower than the HPHC values of the corresponding predicate tobacco products. Therefore, I find that based on the totality of the information provided by the applicant, including but not limited to HPHC and TNCO data, the deficiencies identified in the engineering review have been adequately resolved, and that the applicant has demonstrated that the differences between the new and predicate

tobacco 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).

The new tobacco products are currently in compliance with the FD&C Act. In addition, all of the scientific reviews except the engineering review conclude that the differences between the new and predicate tobacco products are such that the differences do not cause the new tobacco products to raise different questions of public health. As explained above, I concur with all these reviews except the engineering review, 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 SE0013372 - SE0013375 and SE0013384 – SE0013387, as identified on the cover page of this review.