

Technical Project Lead (TPL) Review: SE0007815, SE0007817-SE0007819, SE0007822-SE0007824, SE0007826-SE0007828, SE0007831-SE0007835

SE0007815: Echo Gold King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	19%
Characterizing Flavor	None
SE0007817: Echo Menthol Gold 100 SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	29%
Characterizing Flavor	Menthol
SE0007818: Echo Menthol Gold King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	16%
Characterizing Flavor	Menthol
SE0007819: Echo Menthol King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	Menthol
SE0007822: Echo Red King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	None

SE0007823: Edgefield Gold 100 Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	24%
Characterizing Flavor	None
SE0007824: Edgefield Gold King Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	85 mm
Diameter	7.8 mm
Filter Ventilation	20%
Characterizing Flavor	None
SE0007826: Edgefield Menthol Gold 100 Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	28%
Characterizing Flavor	Menthol
SE0007827: Edgefield Menthol Gold King Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	14%
Characterizing Flavor	Menthol
SE0007828: Edgefield Menthol King Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	Menthol
SE0007831: Edgefield Red King Box	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	None

SE0007832: Exeter Blue 100 SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	40%
Characterizing Flavor	None
SE0007833: Exeter Blue King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	35%
Characterizing Flavor	None
SE0007834: Exeter Gold 100 SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	24%
Characterizing Flavor	None
SE0007835: Exeter Gold King SP	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	20%
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	Xcaliber International LTD, LLC
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Filtered Combusted
Recommendation	
Issue Substantially Equivalent (SE) orders.	

Technical Project Lead (TPL):

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Date: 2018.06.22 11:03:31 -04'00'

Colleen K. Rogers
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: 2018.07.05 06:12:46 -04'00'

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

TABLE OF CONTENTS

1. BACKGROUND	6
1.1. PREDICATE TOBACCO PRODUCTS	6
1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW	9
1.3. SCOPE OF REVIEW	14
2. REGULATORY REVIEW	14
3. COMPLIANCE REVIEW	15
4. SCIENTIFIC REVIEW	15
4.1. CHEMISTRY.....	15
4.2. ENGINEERING	17
4.3. TOXICOLOGY.....	18
5. ENVIRONMENTAL DECISION.....	20
6. CONCLUSION AND RECOMMENDATION	20

1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCTS

The applicant submitted the following predicate tobacco products:

SE0007815: Echo Gold King SP	
Product Name	Echo Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	19%
Characterizing Flavor	None
SE0007817: Echo Menthol Gold 100 SP	
Product Name	Echo Menthol Light 100 SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	29%
Characterizing Flavor	Menthol
SE0007818: Echo Menthol Gold King SP	
Product Name	Echo Menthol Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	16%
Characterizing Flavor	Menthol
SE0007819: Echo Menthol King SP	
Product Name	Echo Menthol King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	Menthol

SE0007822: Echo Red King SP	
Product Name	Echo Full Flavor King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	None
SE0007823: Edgefield Gold 100 Box	
Product Name	Exeter Light 100 SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	24%
Characterizing Flavor	None
SE0007824: Edgefield Gold King Box	
Product Name	Exeter Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	85 mm
Diameter	7.8 mm
Filter Ventilation	20%
Characterizing Flavor	None
SE0007826: Edgefield Menthol Gold 100 Box	
Product Name	Exeter Menthol Light 100 SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	28%
Characterizing Flavor	Menthol
SE0007827: Edgefield Menthol Gold King Box	
Product Name	Exeter Menthol Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	14%
Characterizing Flavor	Menthol

SE0007828: Edgefield Menthol King Box	
Product Name	Exeter Menthol King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	Menthol
SE0007831: Edgefield Red King Box	
Product Name	Exeter Full Flavor King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	0%
Characterizing Flavor	None
SE0007832: Exeter Blue 100 SP	
Product Name	Exeter Ultra Light 100 SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	40%
Characterizing Flavor	None
SE0007833: Exeter Blue King SP	
Product Name	Exeter Ultra Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	35%
Characterizing Flavor	None
SE0007834: Exeter Gold 100 SP	
Product Name	Exeter Light 100 SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.8 mm
Filter Ventilation	24%
Characterizing Flavor	None

SE0007835: Exeter Gold King SP	
Product Name	Exeter Light King SP
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Filter Ventilation	20%
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 22, 2011, Xcaliber International LTD, LLC submitted 15 Substantial Equivalence (SE) Reports. Acknowledgment letters were issued on April 8, 2013. An Advice/Information Request (A/I) letter was issued on April 9, 2013, requesting full identification of the predicate tobacco products, a statement of compliance with requirements of section 907 of the FD&C Act, an environmental assessment, and dates the new tobacco products were first commercially marketed in the United States. The applicant responded to the A/I letter, which was received on May 13, 2013 (SE0008557, SE0008512, SE0008511, SE0008513, SE0008559, SE0008497, SE0008496, SE0008493, SE0008492, SE0008494, SE0008498, SE0008528, SE0008529, SE0008530, SE0008531). On February 11, 2015, FDA issued Notification letters to inform the applicant that scientific review of the SE Reports would commence on March 28, 2015. On March 3, 2015, FDA received an amendment (SE0010937) with updated predicate tobacco product packaging information, which corrects the packaging configuration from "Box" to "Soft Pack" for SE0007823, SE0007824, SE0007826, SE0007827, SE0007828, SE0007831, SE0007832, SE0007833, SE0007834, SE0007835, and commercial marketing evidence of all predicate tobacco products. On March 27, 2015, FDA received an amendment (SE0011056), which provided a listing of revised predicate tobacco products for each of the SE Reports. On March 27, 2015, FDA also received amendments (SE0011057-SE0011071) containing revised versions of the original SE Reports. On April 16, 2015, FDA received an amendment (SE0011680) containing corrections to SE0007818, SE0007819, SE0007824, and SE0007826-SE0007828.

On August 7, 2015, FDA issued an A/I letter. On September 28, 2015, FDA received an extension request (SE0012406) for an additional 45 days to respond to the A/I letter. On October 7, 2015, FDA received the applicant's response (SE0012450) to the August 7, 2015, A/I letter. FDA issued an Extension Denial letter in response to SE0012406 on October 23, 2015. On October 28, 2015, FDA received an amendment (SE0012576) containing the applicant's acknowledgement of the October 23, 2015, Extension Denial letter. On November 20, 2015, FDA received an amendment (SE0012690) further responding to the August 7, 2015, A/I letter and requesting an informal meeting with FDA. On November 20, 2015, FDA also received a request for supervisory review (AP0000015) of the denial of the extension request. On December 11, 2015, and December 22, 2015, FDA held telecons with the applicant to inform them of FDA's decision to deny the informal meeting request. FDA issued an Appeal Denial letter on January 15, 2016.

FDA issued a Preliminary Finding (PFind) letter on January 27, 2016. The applicant responded to the PFind letter on February 25, 2016 (SE0012982). On March 31, 2016, FDA contacted the applicant to request re-submission of four illegible pages in amendment SE0012982. The applicant provided an amendment (SE0013291) containing the four pages, which was received on April 1, 2016. On April 19, 2016, FDA contacted the applicant regarding the February 25, 2016, PFind response. The PFind response stated, "In the event that FDA does not issue a SE order for each of the Products, Xcaliber requests that FDA allow it to change the current paper used in the Products to a new paper within the outstanding provisional SE Reports in order to eliminate the variances that were caused by the initial change from non-FSC to FSC paper." FDA informed the applicant that per the Tobacco Control Act, section 910(a)(1)(B), any modification, such as changing a part or component, in this case the cigarette paper of a tobacco product, will make the product a new tobacco product and inquired whether the applicant would like FDA to create new SE Reports for the new tobacco products containing "new paper." If new SE Reports were to be created, they would be regular SE Reports and not provisional SE Reports. The applicant stated that they were interested in creating new SE Reports for the products containing "new paper" and that they would be in touch with FDA. FDA followed up with the applicant on May 18, 2016, to inquire if they had made a decision regarding the creation of new reports. The applicant expressed their interest once again and informed FDA that they were in the process of gathering the data needed for this process to occur and that they would like to wait until they had sufficient data before creating the new records and starting the next review cycle. The applicant anticipated submitting the data to FDA within the next month; however, to date, no additional communication has occurred with the applicant regarding this topic and no correspondence was received by FDA to establish new SE Reports for this applicant. On May 4, 2018, FDA conducted a telecon to request that the applicant provide clarification to information previously provided in their August 7, 2015, A/I letter (SE0012450) related to packaging materials to ensure accurate identification of the new and predicate tobacco products. On May 15, 2018, FDA received the response to the May 4, 2018, telecon (SE0014723).

Product Name	SE Report	Amendments
Echo Gold King SP	SE0007815	SE0008557 SE0010937 SE0011056 SE0011057 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Echo Menthol Gold 100 SP	SE0007817	SE0008512 SE0010937 SE0011056 SE0011058 SE0011677

Product Name	SE Report	Amendments
		SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Echo Menthol Gold King SP	SE0007818	SE0008511 SE0010937 SE0011056 SE0011059 SE0011680 SE0011751 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Echo Menthol King SP	SE0007819	SE0008513 SE0010937 SE0011056 SE0011060 SE0011680 SE0011751 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Echo Red King SP	SE0007822	SE0008559 SE0010937 SE0011056 SE0011061 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723

Product Name	SE Report	Amendments
Edgefield Gold 100 Box	SE0007823	SE0008497 SE0010937 SE0011056 SE0011062 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Edgefield Gold King Box	SE0007824	SE0008496 SE0010937 SE0011056 SE0011063 SE0011680 SE0011751 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Edgefield Menthol Gold 100 Box	SE0007826	SE0008493 SE0010937 SE0011056 SE0011064 SE0011680 SE0011751 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Edgefield Menthol Gold King Box	SE0007827	SE0008492 SE0010937 SE0011056 SE0011065 SE0011680 SE0011751 SE0012406 SE0012450

Product Name	SE Report	Amendments
		SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Edgefield Menthol King Box	SE0007828	SE0008494 SE0010937 SE0011056 SE0011066 SE0011680 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Edgefield Red King Box	SE0007831	SE0008498 SE0010937 SE0011056 SE0011067 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Exeter Blue 100 SP	SE0007832	SE0008528 SE0010937 SE0011056 SE0011068 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Exeter Blue King SP	SE0007833	SE0008529 SE0010937 SE0011056 SE0011069 SE0011677

Product Name	SE Report	Amendments
		SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Exeter Gold 100 SP	SE0007834	SE0008530 SE0010937 SE0011056 SE0011070 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723
Exeter Gold King SP	SE0007835	SE0008531 SE0010937 SE0011056 SE0011071 SE0011677 SE0012406 SE0012450 SE0012576 SE0012690 SE0012982 SE0013291 SE0014723

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 Nathan Hurley on April 9, 2013, and by Anne Martin on May 27, 2013,¹ and May 31, 2013.²

¹ SE0007815, SE0007817-SE0007819, SE0007822, SE0007823, SE0007826-SE0007828, SE0007831, SE0007832, SE0007834 and SE0007835

² SE0007824 and SE0007833

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 April 27, 2015; April 29, 2015; May 15, 2015; and May 20, 2015, 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.³

4. SCIENTIFIC REVIEW

Scientific reviews were completed by the Office of Science (OS) for the following disciplines:⁴

4.1. CHEMISTRY

Chemistry reviews were completed by Christina Young on July 16, 2015, and by Jiu Ai on November 20, 2015, and April 12, 2016.

The final chemistry review concludes that the new tobacco products have different characteristics related to product chemistry 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 deficiencies in tar, nicotine, and carbon monoxide (TNCO) smoke yields and the addition of (b) (4) to the cigarette paper that have *not* been adequately resolved, but defers these deficiencies to toxicology. The chemistry reviewer determined that the increases in TNCO smoke yields are real differences, and the toxicological implications of these differences are deferred to toxicology. As such, the chemistry review does not identify deficiencies that should be conveyed to the applicant.

The final 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 a chemistry perspective. I do not concur with this conclusion. The outstanding chemistry issues are solely related to the change from non-Fire Standards Compliant (FSC) to FSC cigarette paper. As of 2012, all states in the U.S. have enacted laws requiring cigarettes to meet certain fire standards

³ Addendum reviews were completed on March 27, 2018, to clarify the that characterizing flavor of the predicate tobacco products is "none" or "menthol." The addendum reviews do not change the conclusions of the initial grandfather determinations dated April 27, 2015; April 29, 2015; May 15, 2015; and May 20, 2015.

⁴ SE0012690 was received by FDA on November 20, 2015, and includes additional information to respond to the August 7, 2015, A/I letter. This amendment was not reviewed during 3rd cycle scientific review and this omission was in error. The amendment contains published literature and TNCO test data to support the change from non-FSC to FSC paper. I have reviewed the contents of the amendment and have determined that it does not affect the outcome of the scientific reviews or the determination on these products for substantial equivalence.

for self-extinction when not being smoked. In order to meet this fire standard, tobacco product manufacturers have used different cigarette paper designs to reduce the burn rate of the product (i.e., FSC cigarette paper). Changes in the cigarette paper to meet FSC criteria typically include certain modifications of paper composition and application of extinguishing bands to the paper, in this case, bands comprised of (b) (4). Based on FDA's experience reviewing SE Reports, a consequence of changing from non-FSC to FSC cigarette paper (in the absence of other design or ingredient changes) is an increase in TNCO smoke yields.⁵

As explained in a July 14, 2017, memorandum,⁵ viewed from an overall public health perspective and based on the information available at this time, OS' current thinking is that if the *only* change in a new combusted tobacco product is the change to FSC paper, the new tobacco product incorporating FSC paper does not raise different questions of public health compared to the predicate tobacco product incorporating non-FSC paper. Based on the information provided for tobacco blend, ingredients added to tobacco, and material ingredients in the SE Reports subject of this review, with the exception of the new tobacco products in SE0007817, SE0007822, and SE0007831, the *only* difference between the new and corresponding predicate tobacco products is the change from non-FSC to FSC cigarette paper. Moreover, the increase in TNCO smoke yields for the new tobacco products (ISO: 7-35%; CI: 3-26%) falls within a similar range of TNCO smoke yields seen in other SE Reports⁵ with only non-FSC to FSC cigarette paper changes (ISO: 11-55%; CI: 4-28%). This suggests that the increase in TNCO smoke yields in these particular new tobacco products is due solely to the change to FSC cigarette paper. Based on the forgoing, the addition of (b) (4) to the cigarette paper and increase in TNCO smoke yields in the new tobacco products as compared to the corresponding predicate tobacco products do not cause the new tobacco products in SE0007815, SE0007818, SE0007819, SE0007823, SE0007824, SE0007826-SE0007828, and SE0007832-SE0007835 to raise different questions of public health. Consequently, there are no outstanding deficiencies related to product chemistry for the new tobacco products.

For the new tobacco products in SE0007817, SE0007822, and SE0007831, in addition to the non-FSC to FSC cigarette paper changes described above, the new tobacco products have changes in the tobacco blend. The new tobacco product in SE0007817 has a 1% decrease in (b) (4), the new tobacco product in SE0007822 has a 3% decrease in all tobacco types,⁶ and the new tobacco product in SE0007831 has a 4% decrease in all tobacco types.⁷ Given that there are changes to the tobacco blend in addition to FSC changes to the cigarette paper, we cannot be certain that the increase in TNCO smoke yields is due solely to the change to FSC cigarette paper. However, the changes in tobacco blend are all decreases and are very minor. Generally, if a new tobacco product contains less tobacco than the predicate tobacco product, the new tobacco product exposes consumers to lower levels of nicotine or tobacco-specific nitrosamines (TSNAs) and is not a concern from a chemistry perspective. Moreover, to the extent these changes in tobacco blend lead to increases in TNCO smoke yields, the increases would be very small. Furthermore, the range of TNCO smoke yield increases seen for the new tobacco products in SE0007817, SE0007822, and SE0007831 (ISO: 15-32%; CI: 0-24%) does not exceed the range of TNCO smoke yields seen in other SE Reports⁸ with only non-FSC to FSC

⁵ See July 14, 2017, memo entitled, "Toxicological Implications of FSC Paper"

⁶ All tobacco types includes: (b) (4)

⁷ All tobacco types includes: (b) (4)

⁸ See July 14, 2017, memo entitled, "Toxicological Implications of FSC Paper"

cigarette paper changes (ISO: 11-55%; CI: 4-28%). Since the range of TNCO smoke yield increases is similar to the ranges of other tobacco products where the only change was a change from non-FSC to FSC paper, this suggests that the increase seen for the new tobacco products in SE0007817, SE0007822, and SE0007831 is not due to the tobacco blend change, but rather to the change in paper. Consequently, the change in tobacco blend for the new tobacco products in SE0007817, SE0007822, and SE0007831 does not cause the new tobacco products to raise different questions of public health.

4.2. ENGINEERING

Engineering reviews were completed by Madison Rohrbaugh on June 29, 2015, and November 20, 2015, and by Tiffany Petty on April 8, 2016.

The final engineering review concludes that the new tobacco products have different characteristics related to product design 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 with respect to product engineering. The review identifies the following deficiencies that have *not* been adequately resolved:

1. All of your SE Reports indicate that the base paper porosity decreased by 8% in the new products compared to the corresponding predicate products. A decrease in base paper porosity may increase the concentration of smoke constituents. In the submitted smoke data, the tar, nicotine and carbon monoxide yields increase significantly. Therefore, provide a scientific rationale and justification as to why the decrease in base paper porosity does not cause the new products to raise different questions of public health.
2. SE0007815, SE0007817-SE0007819, SE0007822-SE0007824, SE0007826, SE0007828, SE0007831, and SE0007833-SE0007835 indicate that the puff count increased significantly under the ISO smoking regimen for the new products compared to the corresponding predicate products. This increase in puff count also resulted in significant increases in the TNCO yields for these products. Provide a scientific rationale and justification for why the increases in puff count do not cause the new products to raise different questions of public health.

Therefore, the final 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. I do not concur with this conclusion. The outstanding engineering issues are solely related to the change from non-FSC to FSC cigarette paper. The technological development of FSC cigarettes has focused on modifying the composition and construction of the cigarette paper, in particular by reducing the permeability of cigarette paper to reduce mass burn rate.⁹ The 8% decrease in cigarette base paper porosity in the new tobacco products leads to a reduction of permeability in the FSC cigarette paper. As would be expected for this type of

⁹ See May 18, 2016 memo entitled, "Summary of Literature on Fire Standard Compliant (FSC) Cigarette Paper"

change in product design, there is an increase in TNCO smoke yields. Regarding engineering deficiency 2, a reduced cigarette burn rate, in this case as a result of changing to FSC cigarette paper, results in an increase in the puff count.¹⁰ An increased puff count can result in an increase in TNCO smoke yields.¹¹ As described in section 4.1 of this review, since the only difference between the new and corresponding predicate tobacco products (with the exception of SE0007817, SE0007822, and SE0007831) is the change from non-FSC to FSC cigarette paper, the increase in TNCO smoke yields does not cause the new tobacco products to raise different questions of public health. As explained above and in the noted memo, this is because, viewed from an overall public health perspective, these increases result in less morbidity and mortality as compared to that resulting from household fires starting from cigarettes that do not contain FSC paper. Also, to the extent the changes in tobacco blend in the new tobacco products in SE0007817, SE0007822, and SE0007831 lead to increases in TNCO smoke yields, the increases would be very small. Therefore, the changes do not cause the new tobacco products to raise different questions of public health.

Based on the forgoing, the 8% decrease in cigarette base paper porosity and 2-15% increase in puff count with associated increases in TNCO smoke yields do not cause the new tobacco products to raise different questions of public health. Consequently, there are no outstanding deficiencies related to product engineering for the new tobacco products.

4.3. TOXICOLOGY

Toxicology reviews were completed by Roxana Weil on July 31, 2015, and by Steven Yee on January 4, 2016, and April 21, 2016.

The final toxicology review concludes that the new tobacco products have different characteristics related to product toxicity 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 with respect to product toxicology. The review identifies the following deficiencies that have *not* been adequately resolved:

1. All of your SE Reports indicate that the new products generate higher TNCO yields in the mainstream smoke than the corresponding predicate products. The reference (Werley et al., 2013) you submitted to support a scientific rationale that the higher TNCO yields do not cause the new products to raise different questions of public health is inadequate. It is unclear whether the FSC paper used in Werley et al., 2013 is comparable to the FSC paper (i.e., use of (b) (4)) in the new products. In addition, Werley et al., 2013 has multiple limitations, including, but not limited to, data adjustment via TPM normalization, exclusive use of ISO smoking regimen, failure to fully evaluate mutagenicity and other in vitro studies, and use of underpowered and short-term in vivo study designs that confound toxicological evaluation. Therefore, the

¹⁰ Connolly GN, Alpert HR, Wayne GF, Koh H. Trends in nicotine yield in smoke and its relationship with design characteristics among popular US cigarette brands, 1997-2005. 2007. *Tobacco Control*:16:e5.

¹¹ Although not included in deficiency 2 because the increase was not considered significant, the new tobacco products in SE0007827 and SE0007832 also showed an increase in puff count (4.7% and 2%, respectively) under the ISO smoking regimen and an increase in TNCO smoke yields.

information that you have submitted to address the elevated TNCO levels in the new products as compared to the corresponding predicate products does not support a finding that the new products do not raise different questions of public health from a toxicological perspective. Provide scientific evidence (e.g., data, peer-reviewed articles, and/or other scientifically robust sources of information) and discussion for why increased TNCO levels do not cause the new products to raise different questions of public health. One way to directly address this deficiency is to show that the mainstream smoke yields of the HPHCs (including benzo[a]pyrene) that are of the highest concern in tar are not elevated from the new products compared to the predicate products under ISO and CI smoking regimens. Also show that the volatile HPHCs typically found in the gas phase of smoke (including acetaldehyde, formaldehyde, and benzene) are also not elevated from the new products compared to the predicate products under ISO and CI smoking regimens.

2. All of your SE Reports show that (b) (4) is present in the new products as FSC banding material but not in the corresponding predicate products. The references that you submitted (Theophilus et al. (2007) and Werley et al. (2013)) to demonstrate that (b) (4) in the new products does not raise different questions of public health are insufficient. These referenced studies are not relevant, as there is no evidence that (b) (4) was used in the bands of the FSC paper for these studies. Moreover, these studies have multiple limitations including, but not limited to, data adjustment via TPM normalization, exclusive use of ISO smoking regimen, failure to fully evaluate mutagenicity and other in vitro studies, and use of underpowered and short-term in vivo study designs that confound toxicological evaluation. Hence, the provided information is insufficient to support a determination that the new products do not raise different questions of public health from a toxicology perspective. Provide sufficient evidence (e.g., data, peer-reviewed literature, and/or other scientifically robust sources of information) and scientific discussion that the addition of (b) (4) to the new products does not raise different questions of public health. One way to directly address this deficiency is to provide mainstream smoke yields of the HPHCs which can be generated from burning (b) (4) (e.g., formaldehyde, benzene and benzo[a]pyrene) from the new and predicate products under ISO and CI smoking regimens.

Therefore, the final 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 a toxicology perspective. I do not concur with this conclusion. The outstanding toxicology issues are solely related to the change from non-FSC to FSC cigarette paper. As explained in a July 14, 2017, memorandum,⁵ OS' current thinking is that if the *only* change in a new combusted tobacco product is the change to FSC paper, the new tobacco product incorporating FSC paper does not raise different questions of public health compared to the predicate tobacco product incorporating non-FSC paper. Furthermore, as explained in section 4.1 of this review, the addition of (b) (4) to the cigarette paper and increase in TNCO smoke yields do not cause the new tobacco products to raise different questions of public health. Also, to the extent the changes in tobacco blend in the new tobacco products in SE0007817, SE0007822, and SE0007831 lead to increases in TNCO smoke yields, the increases would be very small. Therefore, the changes do not cause the new tobacco products to raise different questions of

public health. Consequently, there are no outstanding deficiencies related to product toxicology for the new tobacco products.

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 (SE0007815, SE0007817-SE0007819, SE0007822-SE0007824, SE0007826-SE0007828, and SE0007831-SE0007835) 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 differences in characteristics between the new and corresponding predicate tobacco products:

- Cigarette paper is changed to fire standard compliant (FSC) paper with the following characteristics:
 - 4% decrease in cigarette base paper basis weight
 - 8% decrease in cigarette base paper porosity
 - 16% decrease in (b) (4)
 - Addition of (b) (4) bands
- Changes in tobacco blend for the following STNs only:
 - SE0007817: 1% decrease in (b) (4)
 - SE0007822: 3% decrease in all tobacco types
 - SE0007831: 4% decrease in all tobacco types
- Change from soft pack to box for SE0007823, SE0007824, SE0007826-SE0007828, and SE0007831

These differences in characteristics do not cause the new tobacco products to raise different questions of public health. The new tobacco products in SE0007823, SE0007824, SE0007826-SE0007828, and SE0007831 also changed from soft pack to hard pack. This modification does not change the consumable portion of the cigarette, nor is it expected to impact moisture or leach any materials into the new tobacco product. Therefore, this modification does not cause the new tobacco products to raise different questions of public health. The principal difference between the new and corresponding predicate tobacco products, with the exception of the new tobacco products in SE0007817, SE0007822, and SE0007831, is a change from non-FSC to FSC cigarette paper. OS has determined, given the information currently available on the changes that have been observed in HPHC yields as a result of switching from non-FSC to FSC cigarette paper, the benefit of using FSC paper in cigarettes to reduce household fires is anticipated to outweigh any potential increased health risks from the small increases in HPHC exposures that may occur from the use of FSC cigarette paper. Therefore, since the difference between the new and corresponding predicate tobacco products is FSC cigarette paper, 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. For the new tobacco products in SE0007817, SE0007822, and SE0007831, to the extent the changes in tobacco blend lead to increases in TNCO smoke yields, the

increases would be very small and 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).

All of the scientific reviews conclude that the new tobacco products have different characteristics 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. However, as explained above, viewed from an overall public health perspective and based on the information available at this time, the benefit of using FSC cigarette paper outweighs any potential increased health risks from the increase in TNCO smoke yields. Consequently, I 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 (EA) 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 SE0007815, SE0007817-SE0007819, SE0007822-SE0007824, SE0007826-SE0007828, and SE0007831-SE0007835, as identified on the cover page of this review.