Technical Project Lead (TPL) Review:

SE0002985 – SE0002988, SE0002990, SE0002991, and SE0002993 - SE0002997

SE0002985: Smokin Joes Blue 100 Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	None
SE0002986: Smokin Joes Blue 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	None
SE0002987: Smokin Joes Blue King Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002988: Smokin Joes Blue King Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	None
SE0002990: Smokin Joes Gold 100 Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	None

SE0002991: Smokin Joes Gold 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	None
SE0002993: Smokin Joes Menthol 100 Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002994: Smokin Joes Menthol 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002995: Smokin Joes Menthol Gold 100 Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002996: Smokin Joes Menthol Gold 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	Menthol

SE0002997: Smokin Joes Menthol Gold King Size Box Fire Safe	
Package Type	Box
Package Quantity	20 cigarettes
Length	84mm
Diameter	Not provided
Ventilation	Not provided
Characterizing Flavor	Menthol
Common Attributes of SE Reports	
Applicant	Joseph Anderson d/b/a Smokin Joes
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Not Substantially Equivalent (NSE) orders.	

Technical Project Lead (TPL):

Matthew J. Walters -S
2018.10.10 14:24:02 -04'00'

Matthew J. Walters, Ph.D., MPH
CDR, U.S. Public Health Service
Deputy 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: 2018.10.10 15:40:01 -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:

SE0002985: Smokin Joes Blue 100 Size Box Fire Safe	
Product Name	Smokin Joes Ultra Light 100's Box
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002986: Smokin Joes Blue 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Ultra Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	Not provided
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002987: Smokin Joes Blue King Size Box Fire Safe	
Product Name	Smokin Joes Ultra Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	8.23 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002988: Smokin Joes Blue King Size Soft Pack Fire Safe	
Product Name	Smokin Joes Ultra Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	8.23 mm
Ventilation	Not provided
Characterizing Flavor	None

SE0002990: Smokin Joes Gold 100 Size Box Fire Safe	
Product Name	Smokin Joes Light 100's Box
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002991: Smokin Joes Gold 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	None
SE0002993: Smokin Joes Menthol 100 Size Box Fire Safe	
Product Name	Smokin Joes Menthol 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002994: Smokin Joes Menthol 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Menthol 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	Menthol

SE0002995: Smokin Joes Menthol Gold 100 Size Box Fire Safe	
Product Name	Smokin Joes Menthol Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002996: Smokin Joes Menthol Gold 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Menthol Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	Menthol
SE0002997: Smokin Joes Menthol Gold King Size Box Fire Safe	
Product Name	Smokin Joes Menthol Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.91 mm
Ventilation	Not provided
Characterizing Flavor	Menthol

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 22, 2011, FDA received 11 SE Reports (SE0002985 - SE0002988, SE0002990, SE0002991, and SE0002993 - SE0002997) from Joseph Anderson d/b/a Smokin Joes (Smokin Joes). FDA issued Acknowledgment letters for SE0002985 – SE0002988 on August 24, 2011, and for SE0002990 - SE0002997 on August 31, 2011. On June 4, 2012, FDA corresponded via fax requesting the applicant to identify any inaccuracies or omissions for each proposed tobacco product name and corresponding STN.[1] On June 8, 2012, FDA received the applicant's amendment (SE0004569) in response to the June 4, 2012, fax. On November 8, 2012, and November 20, 2012, FDA conducted teleconferences, as part of FDA data clean-up process, to clarify tobacco product names and identify discontinued tobacco products.

[1] The applicant included the June 4, 2012, FDA fax correspondence in its amendment SE0004569.

On October 31, 2012, Public Health Impact (PHI) reviews were completed, and these SE Reports were assigned to PHI Tier 1. Upon further review of the product composition, FDA reassigned all of the products to PHI Tier 2 on May 9, 2013.

On December 28, 2012, FDA issued Advice/Information (A/I) Request letters for these SE Reports.[2] On January 18, 2013, FDA received a 30-day extension request (SE0006310) to respond to the December 28, 2012, A/I Request letters. On January 31, 2013, FDA conducted a teleconference to inform the applicant that the responses to the December 28, 2012, A/I Request letters would not be due by January 27, 2013, and that FDA would be issuing a letter with further instructions.[3] On February 28, 2013, FDA received amendments (SE0007496 - SE0007506) in response to the December 28, 2012, A/I Request letters.

On March 4, 2013, FDA emailed Smokin Joes to request further clarification of tobacco product names and to specify package type and package quantity for all SE Reports. On March 19, 2013, FDA received an amendment (SE0009117) in response to the March 4, 2013, email.

On July 9, 2013, FDA issued a Correction letter informing Smokin Joes that FDA had revised the records to include clarifications to the new tobacco product names. On July 31, 2013, FDA received an amendment (SE0009439) in response to the July 9, 2013, Correction letter, which also addressed a voicemail and several e-mails from the Office of Compliance and Enforcement regarding clarification of the grandfathered predicate tobacco product names.

On February 11, 2015, FDA issued a Notification letter informing Smokin Joes that scientific review of these SE Reports would begin on March 28, 2015. On March 27, 2015, FDA received an amendment (SE0011072) in response to the February 11, 2015, Notification letter, which included amended design features, ingredients, and materials data, grandfathered predicate tobacco product information, and new tobacco product information. On January 27, 2016, FDA received a 90-day extension request (SE0012816) for FDA to delay taking action on Smokin Joes' SE Reports. FDA issued a General Correspondence letter on March 11, 2016, stating there is no basis for an extension request since there is no timeframe for response currently requested in an A/I Request letter or a Preliminary Finding (Pfind) letter.

On November 23, 2016, FDA issued a General Correspondence letter, so that the applicant could provide information to fully characterize the new and corresponding predicate tobacco products

[2] Smokin Joes identified that SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 had a change in [redacted] A new tobacco product includes "any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery, or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007." Section 910(a)(1)(B) of the Federal Food, Drug and Cosmetic Act. The information provided by the applicant during review is insufficient to determine whether the manufacturing process change modifies the tobacco products that are the subject of SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997. To the extent that the manufacturing change modifies those products and thus results in new tobacco products, such new tobacco products would not have been first introduced or delivered into interstate commerce for commercial distribution after February 15, 2007, and prior to March 22, 2011 and thus, unless grandfathered, could not be legally marketed without first undergoing premarket review. Section 910(a)(2) of the FD&C Act. See section 4.1 of this memorandum discussing the application of menthol to the new products.

[3] A notification letter issued later with instructions regarding amendments and the start of the substantive scientific review process.

for SE0002985 - SE0002997.[4] On March 10, 2017, FDA received a partial response (SE0013970) to the November 23, 2016, General Correspondence letter, and certificates of analysis (SE0013969). On March 24, 2017, FDA received an unsolicited amendment (SE0013992) requesting a 120-day extension of time to provide a complete response to the November 23, 2016, General Correspondence letter; the applicant stated that the extension request was due to incomplete new tobacco product testing by a third-party testing laboratory. On June 16, 2017, FDA issued a General Correspondence letter, granting the applicant until July 10, 2017, to respond to the November 23, 2016, General Correspondence letter.

On July 10, 2017, FDA received an amendment (SE0014198) in response to the June 16, 2017, General Correspondence letter. On October 5, 2017, FDA issued an A/I Request letter with a response due date of December 4, 2017. On October 19, 2017, FDA received an amendment (SE0014381) requesting an extension to respond to the October 5, 2017, A/I Request letter. On November 8, 2017, FDA denied this extension request. No response was received from the applicant by the A/I Request letter response due date of December 4, 2017. A PFind letter, conveying all required and requested deficiencies included in the October 5, 2017, A/I Request letter, was issued on March 5, 2018, with a response due date of April 4, 2018. To date, no response to the March 5, 2018, PFind letter has been received. On February 15, 2018, FDA held a follow-up telecon in which Smokin Joes stated they would not be able to respond to any deficiency letters prior to a meeting with FDA on March 7, 2018. Smokin Joes noted they intended to gain advice for all deficiency letters during this March 7, 2018 meeting. Although the meeting was held, to date FDA has not received any response to deficiency letters for these STNs.

Product Name	SE Report	Amendments
Smokin Joes Blue 100 Size Box Fire Safe	SE0002985	SE0004569 SE0006310 SE0007496 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

[4] The General Correspondence letter acknowledges that requested information is similar to the August 19, 2016, PFind letter and September 7, 2016, A/I Request letter, which were issued to SE Reports of other Smokin Joes' batches.

Smokin Joes Blue 100 Size Soft Pack Fire Safe	SE0002986	SE0004569 SE0006310 SE0007497 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Blue King Size Box Fire Safe	SE0002987	SE0004569 SE0006310 SE0007498 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Blue King Size Soft Pack Fire Safe	SE0002988	SE0004569 SE0006310 SE0007499 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Gold 100 Size Box Fire Safe	SE0002990	SE0004569 SE0006310 SE0007500 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

Smokin Joes Gold 100 Size Soft Pack Fire Safe	SE0002991	SE0004569 SE0006310 SE0007501 SE0009117 SE0009439 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Menthol 100 Size Box Fire Safe	SE0002993	SE0004569 SE0006310 SE0007502 SE0009117 SE0009439 SE0009929 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Menthol 100 Size Soft Pack Fire Safe	SE0002994	SE0004569 SE0006310 SE0007503 SE0009117 SE0009439 SE0009929 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

Smokin Joes Menthol Gold 100 Size Box Fire Safe	SE0002995	SE0004569 SE0006310 SE0007504 SE0009117 SE0009439 SE0009929 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Menthol Gold 100 Size Soft Pack Fire Safe	SE0002996	SE0004569 SE0006310 SE0007505 SE0009117 SE0009439 SE0009929 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Menthol Gold King Size Box Fire Safe	SE0002997	SE0004569 SE0006310 SE0007506 SE0009117 SE0009439 SE0009929 SE0011072 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

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 Dan Gonski on December 28, 2012, and April 22, 2013.

These initial reviews concluded that the SE Reports are administratively incomplete because the heating source of the new and predicate products was not included in the SE Reports.

However, this information was provided during the scientific review process. Therefore, 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 March 4, 2015, April 27, 2015, April 29, 2015 and April 25, 2018 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.

4. SCIENTIFIC REVIEW

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

4.1. CHEMISTRY

A chemistry review was completed by Kimberly Agnew-Heard on July 14, 2015. A memo to file was completed by Jikun Liu on August 25, 2017, updating the chemistry review in order to review amendments received in response to the General Correspondence letter after the review was finalized.

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 the following deficiencies[5] that have *not* been adequately resolved:

1. All of your SE Reports provide information about tobacco and ingredients added to tobacco in the new and predicate products, but limited information on the grades were provided. For example, all of your SE Reports list "see attached letter from supplier" for the grade and purity of ingredients(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) (b) (4) in the new and predicate products; however, this information is not included in the attachments. All of your SE Reports list subcomponent ingredients of the (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4); however, functions of most individual ingredients are missing. The predicate products in SE0002993 –

[5] In addition to deficiencies, the review identifies requests. Because requests do not impact the determination of substantial equivalence, they are not included in this TPL review.

SE0002997 used (b) (4)] The purity and form were not reported for the two types of menthols. Without this information, we cannot determine whether the new and predicate products are substantially equivalent. Additionally, the information provided for tobacco does not include sufficient detail to fully identify the composition of the new and predicate products. For example, we are unable to understand the meaning of the tobacco grades (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) (b) (4) blend of the new product or (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) . Furthermore, (b) (4)(b) (4) " are listed twice for all the new and predicate products, respectively. It is not clear why one grade is listed twice within the same type of tobacco. Moreover, all of your SE Reports list (b) (4) in the new products and (b) (4) in the predicate products but lack the ingredients used to process the (b) (4) t (b) (4) . We need additional information that uniquely identifies the tobacco used in the new and predicate products to ensure that the tobacco and other ingredients used in the new and predicate products are equivalent for both products[6]. If you use a tobacco grading system, it would be helpful to know the tobacco grade (along with an explanation of the grading system) for each type of tobacco used in the new and predicate products. Provide a detailed list including:

a. Uniquely identifying information for all ingredients (e.g., CAS #, grade/purity, function)
b. Uniquely identifying information for all tobacco (e.g., tobacco grading system)

If a difference exists between the new and corresponding predicate products, provide a rationale for each difference with evidence and a scientific discussion for why the difference does not cause the new product to raise different questions of public health.

2. All of your SE Reports lists mainstream smoke yields of TNCO and three HPHCs (acetaldehyde, benzene and B[a]P) under ISO and CI smoking regimens. However, there are discrepancies between the data sets in the GLS Report and Exhibit A of the July 10, 2017 amendment. For example, in the GLS report, nicotine level in mainstream smoke under ISO regimen is 1.85 mg/cig for the new products of SE0002990 and SE0002991, while Exhibit A shows that the value is 1.69 mg/cig. In the GLS report, nicotine level in mainstream smoke under CI regimen is 3.94 mg/cig for the new products of SE0002990 and SE0002991, while the quantity in Exhibit A is 3.51 mg/cig. Explain the data discrepancies in your amendment and identify the correct data sets for FDA to determine whether the HPHC yield differences may cause the new products to raise different questions of public health.[7]

[6] The deficiency requires some clarification, as this information is not needed to show that the ingredients are "equivalent" but rather to assess whether there are any differences between the new and predicate product and, if so, to determine whether those differences do not cause the new product to raise different questions of public health.
[7] This sentence has been corrected to read "Explain the data discrepancies in your amendment and identify the correct data sets for FDA to determine whether the differences in HPHC yields do not cause the new products to raise different questions of public health." The letter-ready deficiencies have been modified accordingly.

3. All of your SE Reports contain some quantities of ingredients that require additional explanation. For example, in the amendment dated March 26, 2015, the values of (b) (4)(b) (4)(b) (4)(b) (4)(b) (4) in seam adhesive are reported as (b) (4) mg/cigarette and (b) (4) mg/cigarette for the new and predicate products respectively and the quantities of (b) (4)(b) (4)(b) (4)(b) (4)(b) (4) in tipping adhesive are (b) (4) mg/cigarette for the new products. In addition, some quantities of ingredients are presented as shaded cells in the Excel sheets. The significance of the shaded cells is not evident. Provide absolute quantities instead of value ranges and clarify the meaning of shaded cells in your SE Reports. If the values in the shaded cells are assumed to be zero, "Design Features" data set indicates that the (b) (4)(b) (4) levels of the new products are 188% or 243% higher than those of the predicate products, while "Tobacco Blends" data set shows that the new products do not contain (b) (4)(b) (4) but the predicate products have (b) (4) mg/cigarette of the ingredient. Explain the discrepancy in (b) (4)(b) (4) level of tobacco blend for the new and predicate products.

4. All of your SE Reports provide (b) (4)(b) (4) information in the ingredient list of (b) (4) concentrate in the Excel spreadsheets in the amendment dated March 26, 2015; however, the ingredient appears twice with two different concentrations in the same list. Explain the purpose of listing the ingredient twice and identify its correct concentration.

5. All of your SE Reports compared the HPHC data of the "present day predicates" to that of the new products. You imply that the "present day predicates" were constructed with the same materials and components as all the Smokin Joes products marketed on February 15, 2007. A present day predicate product is a product that is remanufactured at the present day consistent with the product composition (e.g., tobacco, ingredients other than tobacco, and materials) and design specifications in place at the time the grandfathered predicate product was originally manufactured. However, you did not submit documentation demonstrating that the manufacture of the predicate products at present day reflects the grandfathered predicate product at the time of the original manufacture. Confirm whether there is any difference between the "present day predicates" and corresponding grandfathered predicate products. If inconsistency difference exists in product composition and design parameters between the "present day predicates" and corresponding predicate products, provide detailed information of the difference for FDA to determine whether the "present day predicates" are reflective of the grandfathered predicate products for all SE Reports. For example, if there is a difference in tobacco grade, provide information on the tobacco grades and grading system. Also, provide a rationale for each difference with evidence and a scientific discussion for why the difference does not cause the new products to raise different questions of public health.[8]

6. All of your SE Reports include data comparing the quantities of HPHCs in the new and remanufactured predicate products. However, your SE Reports lack detailed information of methods, which is necessary to fully evaluate the data. Provide the

[8] This sentence is included in error, and has been removed from the letter-ready deficiencies.

following information about the HPHC testing so that we can fully evaluate the HPHC data:

a. Reference product datasets (e.g., 1R6F).
b. Quantitative test protocols and method used.
c. A summary of the results for all testing performed.

If your test methods are national or international test standards, identify any deviations from those standards. For example, you provided methods (b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4). These methods appear to be based on Coresta and BAT methods. However, it is unclear if your methods have any differences from the Coresta and BAT methods. Provide a list of deviation(s) for each method. If there are no deviations, state as such.

7. SE0002993 – SE0002997 state the manufacturing process has changed and that the (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) as of October 15, 2012. However, your SE Reports SE0002993 – SE0002997 list (b) (4)(b) (4)(b) (4)(b) (4) as (b) (4) mg/cigarette in the new products and 5 - 7.5 mg/cigarette in the predicate products. Clarify the manufacturing process for adding menthol for each new and predicate product and submit new detailed ingredient information for the filter and tobacco for each new and predicate product affected by this manufacturing change. In addition, changes in menthol quantities applied to different locations of a cigarette could result in changes in menthol yields in mainstream smoke that could cause the new products to raise different questions of public health. Provide the absolute quantities of menthol as mg/cigarette in the new and predicate products as well as identify the component that menthol is added. If there is a difference in quantities or application of menthol between the new and corresponding predicate products, provide scientific evidence and rationale why this difference in menthol content does not cause the new products to raise different questions of public health. One way to address this concern is to measure menthol yields in mainstream smoke of the new and predicate products under both the ISO and Canadian Intense smoking regimens. If the menthol yields are different, explain why the difference does not cause the new products to raise different questions of public health.[9]

[9] (b) (5) . Menthol is a volatile compound that is known to redistribute between tobacco filler and filter material until an equilibrium concentration is obtained. The redistribution occurs within the first several weeks and results in a consistent menthol content for all cigarettes within a package. However, changes in the total concentration of menthol in a package may result in changes in the amount of menthol in the smoke. The applicant did not provide data or scientific rationale to demonstrate a change in menthol content does not cause the new tobacco products containing menthol to raise different questions of public health. Changes relating to menthol were not evaluated by the Behavioral and Clinical Pharmacology (BCP) reviewer. The available literature focuses on the comparison between non-mentholated relative to mentholated cigarettes, as opposed to differences in menthol levels (as is the case for the new and predicate products here). Therefore, at this time, based on the available scientific evidence, the change in menthol content between the new and predicate products do not cause the new products to raise different questions of public health. Thus, this deficiency relating to menthol should not be conveyed to the applicant.

8. All of your SE Reports list individual ingredients within the following complex ingredient quantities as percentages but do not specify the original units of the numerator and denominator, or define the denominator:

    a. Casings
    b. Top flavors
    c. Plug wraps
    d. Cold glue
    e. Hot melt
    f. Printing materials
    g. Blue monogram ink

    In order for us to fully understand the composition of the new and predicate products and make a determination of substantial equivalence, provide ingredient quantities as mass per unit of use (e.g., mg/cigarette).

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 a chemistry perspective.

4.2. ENGINEERING

An engineering review was completed by Beth Tirio on July 13, 2015. A memo to file was completed by James Roche on September 21, 2017, updating the engineering review in order to review amendments received in response to the General Correspondence letter after the review was finalized.

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 the differences do not cause the new tobacco products to raise different questions of public health. The review identifies the following deficiencies[10] that have *not* been adequately resolved:

1. All of your SE Reports provide information on the design parameters for the new and predicate products. However, your SE Reports do not include all of the design parameters necessary to fully characterize the new and predicate products. In order to adequately characterize the products, it is necessary to compare key design parameters. Provide the target specification and upper and lower range limits for all of the following cigarette design parameters for each new and predicate product:

    a. Tobacco moisture (%)
    b. Filter pressure drop (mm H_20)
    c. Filter ventilation (%)
    d. Cigarette draw resistance (mm H_2O)

[10] In addition to deficiencies, the review identifies requests. Because requests do not impact the determination of substantial equivalence, they are not included in this TPL review.

e. Filter denier per filament (DPF)
f. Filter total denier (g/9000 m)
g. Filter length (mm) [target specification for SE0002988 new product only and range limits for all new and predicate products]

Provide the upper and lower range limits for all of the following cigarette design parameters for each new product:

h. Cigarette paper band porosity (CU)

Provide the upper and lower range limits for all of the following cigarette design parameters for each predicate product:

i. Cigarette diameter (mm)

For each of the above parameters, provide the necessary data on a per unit of product basis (e.g., filter length should be reported in mm per cigarette). If a design parameter is not applicable (e.g., band porosity if the cigarette paper does not contain bands), state as such and provide a scientific rationale.

If a difference exists between the new and corresponding predicate products, provide a rationale for each difference in the target specification and range limits with evidence and a scientific discussion for why the difference does not cause the new product to raise different questions of public health.

Note that denier per filament and total denier are necessary because filter efficiency (%) was not provided. As an alternate to submitting the information described above for denier per filament and total denier, you may provide target specification and upper and lower range limits for filter efficiency.

2. All of your SE Reports do not provide complete test data for the new and predicate products. You stated that you remanufactured the predicate product and, therefore, are able to provide the necessary design parameter data. Even if you no longer manufacture the predicate product, you still need to fully characterize the new and predicate products and, if the characteristics are different, demonstrate that the new products do not raise different questions of public health. Provide full test data (including test protocols, quantitative acceptance criteria, data sets, and a summary of the results) for all of the following design parameters for each new and predicate product:

a. Puff count
b. Cigarette draw resistance (mm H_2O)
c. Tobacco filler mass (mg)
d. Tobacco moisture (%)
e. Cigarette paper base paper basis weight (g/m^2)
f. Cigarette paper base paper porosity (CU)
g. Cigarette paper band porosity (CU)
h. Denier per filament (DPF)

i. Total denier (g/9000m)
j. Filter ventilation (%)
k. Filter density (g/cm^3)
l. Filter pressure drop (mm H_2O)

For each of the above parameters, provide the necessary data on a per unit of measurement of product basis (e.g., filter pressure drop should be reported in mm H_2O per cigarette). If a design parameter is not applicable (e.g., band porosity, if the cigarette paper does not contain bands), state as such. One potential option for obtaining data on the predicate products includes, but is not limited to:

- Manufacture the predicate products at present day, consistent with the product composition and design specifications in place at the time the grandfathered predicate product was originally manufactured. In this case, design parameter data should be accompanied by documentation demonstrating that the manufacture of the predicate product at present day is reflective of the grandfathered predicate product at the time of original manufacture.

Certificates of analysis (COAs) from the material supplier may satisfy this deficiency. If you choose to address this deficiency by providing COAs for any of the parameters listed above, the COAs must include a target specification, quantitative acceptance criteria, parameter units, test data average value, and either the standard deviation of the test data or the minimum and maximum values of the test data. The COAs must be a complete, unaltered COA from the material supplier.

Additionally, for the design parameters listed above that were tested according to national or international standards, identify the standards and state what deviations, if any, from the standards occurred.

3. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 indicate that the new and predicate products have multiple materials, including cigarette paper base paper materials. In accordance with section 910(a)(1)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), each product modification, including use of an alternate material, constitutes a new tobacco product. A material is an alternate material if it has any difference in composition (e.g., ingredients, additives, and biological organisms), or design parameters (target specifications or range limits).[11] Each identified new and predicate product must consist of a single combination of cigarette paper base paper materials. Identify the following:

[11] This sentence warrants correction and clarification. A new tobacco product includes any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007. Section 910(a)(1)(B) of the FD&C Act. A difference in design parameter that does not modify the tobacco product, e.g., a tightening of a design parameter range, does not result in a new tobacco product. This deficiency has been edited to reflect the foregoing in the letter-ready comments.

a. Every unique material combination in the predicate product that you are comparing to the new product in accordance with Section 910(a)(2)(B) of the FD&C Act.[12]
b. Every unique material combination in the new tobacco product under Section 905(j)(2) of the FD&C Act. Each specific combination of materials will be considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.[13]

Provide the list of ingredients and ingredient quantities for each identified material in each new and predicate product.

Provide the target specifications and upper and lower range limits for all of the following design parameters for each material in each new and predicate product:

c. Cigarette paper base paper basis weight
d. Cigarette paper base paper porosity
e. Cigarette draw resistance

Provide the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for *all* of the following design parameters for each material in each new and predicate product:

f. Cigarette paper base paper basis weight
g. Cigarette paper base paper porosity
h. Cigarette draw resistance

COAs from the material supplier may satisfy this portion of the deficiency. If you choose to address this deficiency by providing COAs for any of the parameters listed above, the COAs must include target specification; quantitative acceptance criteria; parameter units; test data average value; and either the standard deviation of the test data or the minimum and maximum values of the test data. The COA must be a complete, unaltered COA from the material supplier.

Additionally, if a difference exists between the new and predicate product identified for each SE Report, provide justification for the difference and a scientific rationale for why the difference does not cause the new product to raise different questions of public health. Some options for demonstrating that the differences do not cause the new products to raise different questions of public health include the following:

Option 1: Identify a single unique predicate product (with corresponding ingredients), composed of a single cigarette paper base paper material. Additionally, select and identify a single new product (with corresponding ingredients), composed of a single cigarette paper base paper material. The

[12] The statutory references in this sentence are incorrect and were included by the third cycle engineering reviewer in error. The letter-ready deficiencies have been edited to remove the statutory reference.
[13] Same as note above.

identified new product will be the only version of the new product considered for evaluation of substantial equivalence with the identified predicate product. The identified new product will also be the only material combination permitted. Therefore, alternate materials will not be permitted. Provide target specifications, upper and lower range limits, and test data generated from testing of cigarette paper base paper basis weight, cigarette paper base paper porosity and cigarette draw resistance and HPHCs for the unique new and predicate products, based on the single combination of cigarette paper base paper materials identified. If a difference exists between the single identified new product and the single identified predicate product, provide scientific evidence and a rationale for why the difference does not cause the new product to raise different questions of public health.

Option 2: If you need to list alternate materials for the new and predicate products, you may choose to demonstrate that the use of alternate cigarette paper base paper materials does not cause the new products to raise different questions of public health. To do this, identify every unique new and predicate product that may result from the integration of each combination of alternate materials. Each identified new and predicate product must consist of a single cigarette paper base paper material combination. Provide target specifications, upper and lower range limits, and test data generated from testing of cigarette paper base paper basis weight, cigarette paper base paper porosity and cigarette draw resistance and HPHCs for each identified new and predicate product, based on all possible combinations of cigarette paper base paper materials. If a difference exists between the new and predicate products identified for each SE Report, provide scientific evidence and a rationale for why the difference does not cause the new product to raise different questions of public health.

Option 3: If you need to list alternate materials for the new and predicate products, you may choose to provide a "bracketing" approach to demonstrate that the alternate materials in the new and predicate products do not cause the new products to raise different questions of public health. To do this, specify two unique versions[14] of the new product, and if the predicate product contains alternate materials, two unique versions of the predicate product:

- For one of the unique versions of the new product, identify a single set of alternate materials that result in the highest HPHC yields generated through integration of the alternate materials.
- For the other unique version of the new product, identify a single set of alternate materials that result in the lowest HPHC yields generated through integration of the alternate materials.
- For one of the unique versions of the predicate product, identify a single set of alternate materials that result in the highest HPHC yields generated through integration of the alternate materials.

[14] To clarify, the phrasing "two unique versions of the new tobacco product" is not intended to suggest that the use of alternate materials would not result in multiple tobacco products. Rather, the phrasing is used only for convenience/instruction.

- For the other unique version of the predicate product, identify a single set of alternate materials that result in the lowest HPHC yields generated through integration of the alternate materials.

Provide a justification for why each version of the new and predicate product is representative of the highest and lowest HPHC yield in the products. Additionally, for each version specified, provide target specifications, upper and lower range limits, and test data generated from testing of cigarette paper base paper basis weight, cigarette paper base paper porosity and cigarette draw resistance and HPHCs for all of the identified new and predicate products. If a difference exists between the identified new and predicate products, provide scientific evidence and a rationale for why the difference does not cause the new product to raise different questions of public health.

All predicate product materials selected or used for comparison or bracketing must have been used in the predicate tobacco product as of February 15, 2007 and have been commercially marketed (other than for test marketing).

4. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 provide contradictory design parameter information between the original submission and the corresponding Excel spreadsheet of the March 26, 2015 amendment. This prevents the complete product characterization of the design parameters. If there is a discrepancy between the value provided in the original submission and the other amendments, clearly state which is correct. Clearly state the correct target specification for the following design parameters of the listed SE Reports and products:

    a. SE0002985, SE0002986, SE0002990, and SE0002991: Overall cigarette length for predicate products only
    b. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997: Overall cigarette diameter for new products only
    c. SE0002985, SE0002986, SE0002990, and SE0002991: Filter length for predicate products only

5. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 provide inconsistent information regarding the new and predicate product cigarette paper base paper porosity. In the original submissions, you use “g” as the unit of measure for the cigarette paper base paper porosity. This is not an accepted porosity unit of measure. Report the cigarette paper base paper porosity using the accepted porosity unit of measure (CU). If there is a discrepancy between the value provided in the original submission and the other amendments, clearly state which is the correct target specification using the accepted porosity unit of measure (CU).

6. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 provide the new product “Band Porosity (CU)/Band Diffusion (cm/s)” target specifications in the March 26, 2015 amendment using “cm/s” as the unit of measure. Based on the data label, this implies that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, these SE Reports provide the new product cigarette paper band porosity using “g” as the unit of

measure. This is not an accepted porosity unit of measure. Clearly report the correct new product cigarette paper band porosity for all SE Reports using the accepted porosity unit of measure (CU).

7. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 report the new and predicate product filter ventilation target specifications in the original submission as <1%. This is not an exact value and prevents the complete characterization of the new and predicate products. Furthermore, in the March 26, 2015 amendment, you report the "Tip Ventilation Rate" for all new and predicate products. It is unclear if "Tip Ventilation Rate" is intended to represent filter ventilation. Clarify the use of "Tip Ventilation Rate" and, if it is intended to represent filter ventilation, clearly report the correct, exact target specifications for all new and predicate products.

8. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997 include inconsistent tipping paper information. In your March 26, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is identified as 26 mm, 30 mm, or 35 mm, depending on the SE Report and product. If the tipping paper is 27 mm, as reported in the March 26, 2015 amendment, provide a rationale as to why it is not long enough to cover the 30 mm filter in SE0002985, SE0002986, SE0002990, SE0002991, or SE0002993 – SE0002996. Furthermore, in the original submissions for SE0002985 – SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997, the tipping paper 'length' is identified as 26 mm, 30 mm, or 35 mm, depending on the SE Report and product. It is unclear if the values reported in the original submission or the values reported the other amendments are in fact the correct tipping paper lengths. Additionally, if you intended to report the tipping paper 'width' as the 'length' in the March 26, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the March 26, 2015 amendment and the original submission for the predicate products in SE0002985, SE0002986, SE0002990, and SE0002991. For SE0002985 – SE0002986, SE0002988, SE0002990, SE0002991, SE0002993 – SE0002997, provide the tipping paper length target specifications for the new and predicate products.

9. All of your SE Reports include information on the tobacco filler mass and tobacco rod density of the new and predicate products. However, you do not adequately characterize either design parameter. For the tobacco filler mass of all new products and the tobacco rod density of all predicate products, you state that the data provided is "based on data from scientific consultant's physical analysis of samples of the product." Thus, the target specifications and upper and lower range limits provided reflect a sample of the actual manufacturing outcome, rather than the target and range limits of the manufacturing process. Furthermore, all reported predicate product filler mass target specifications are approximations. An exact target specification is needed in order to accurately compare the new and predicate products and determine if the new product raises different questions of public health. Provide the exact target specification and upper and lower range limits for the tobacco filler mass (mg) and tobacco rod density (g/cm^3) for all new and predicate products.

10. All of your SE Reports contain incomplete band spacing and band width information for the new product. You provide a data label which lists both design parameters; however, only one target specification and one set of upper and lower range limits is provided. It is unclear which design parameter is associated with the data. Clearly state the target specification and upper and lower range limits for both the band spacing and band width of all new products.

11. All of your SE Reports contain inconsistent information regarding the filter design parameters. You provide denier information for the new and predicate products (labeled as "Total Denier / Denier per Filament") indicating that the total denier is [redacted] or [redacted], depending on the SE Report and product, and the denier per filament is [redacted]. Because total denier is the mass of 9000 m of tow, this value is typically in the thousands. It is unclear which values are in fact the correct denier values. Clarify the discrepancy and provide the target specification and upper and lower range limits for all new and predicate products.

12. All of your SE Reports include information for the filter density of the new and predicate products. However, the upper and lower range limits for the predicate products require additional clarification. For all predicate products, the range limits vary between [redacted] g/cm^3 and [redacted] g/cm^3, depending on the product. A lower range limit less than zero is not possible. In addition, your March 10, 2017 Amendment states that Exhibit B- 2 provides a [redacted] COA but this exhibit lacks filter density information. Review the predicate product target specifications and upper and lower range limits and report the correct value, as the lower range limit would result in a negative value. Additionally, if a difference exists between the new and predicate product target specifications or upper and lower range limits identified for each SE Report, provide justification for the difference and a scientific rationale for why the difference does not cause the new product to raise different questions of public health.

13. All of your SE Reports include information on the filter design parameters of the new and predicate products. However, some of your SE Reports indicate design parameter differences that require additional information in order to adequately characterize the design parameters. You provide a limited explanation for these differences without a discussion on the impact to public health. Therefore, provide a rationale with evidence and a scientific discussion of why the differences do not raise different questions of public health for each of the following topics:

    a. In SE0002987, SE0002988, and SE0002997, the filter pressure drop decreased 11% in the new products as compared to the corresponding predicate products. For SE0002987, SE0002988, and SE0002997, the CO and nicotine levels are higher in the new products as compared to the corresponding predicate products. Also for SE0002988, the tar level is higher in the new products as compared to the corresponding predicate products.
    b. In SE0002987, and SE0002997, the filter length of the new product decreased by 20% in the new products as compared to the corresponding predicate products. For SE0002987 and SE0002997, the CO and nicotine levels are higher in the new products as compared to the corresponding predicate products.

c. In SE0002987 and SE0002997, the filter pressure drop and filter length decreased in the new products as compared to the corresponding predicate products. For SE0002987 and SE0002997, the CO and nicotine levels are higher in the new products as compared to the corresponding predicate products.

14. All of your SE Reports provide average values for puff count for all of the new and predicate products. You do not provide test protocols or data sets. Complete test data is necessary to fully characterize the new and predicate products for evaluation of substantial equivalence. Accordingly, provide the test protocol and data sets for puff count for all of your new and predicate products. Additionally, for all SE Reports *except* SE0002995 and SE0002996, the puff count of the new products is between 16% and 43% higher than the puff count of the predicate products. For all SE Reports except SE0002995 and SE0002996, nicotine is a higher in the new products as compared to the corresponding predicate products. For SE0002987, SE0002988, and SE0002997, the CO and nicotine levels are higher in the new products as compared to the corresponding predicate products. For SE0002988, the tar level is higher in the new products as compared to the corresponding predicate products. Provide scientific justification for why the difference in puff count for all SE Reports except SE0002995 and SE0002996 does not cause the new products 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.

4.3. TOXICOLOGY

A toxicology review was completed by James Hobson on September 16, 2016. A memo to file was completed by Yanling Chen on September 1, 2017, updating the toxicology review in order to review amendments received in response to the General Correspondence letter after the review was finalized.

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. The review identifies the following deficiencies that have *not* been adequately resolved:

1. All of your SE Reports except SE0002993 and SE0002994 indicate apparent increases[15] in the following HPHCs, relative to the corresponding remanufactured predicate products:

[15] I agree with Chemistry deficiencies 2 and 6, which explain why the HPHC data submitted by the applicant is inadequate and cannot be used to identify differences in HPHC yields between the new and predicate tobacco products. While the submitted data cannot be relied on to determine if there are actual differences in HPHC yields, the submitted data shows increases in HPHC yields (referred to here as "apparent increases"). The applicant did not explain why these apparent increases in HPHC yields do not cause the new products to raise different questions of public health. This toxicology deficiency should be edited to discuss the apparent increases in HPHCs. The edits will be made in the letter ready deficiencies that are to be conveyed to the applicant.

- SE0002985 and SE0002986: CO, and B[a]P
- SE0002987 and SE0002988: CO, acetaldehyde, benzene, B[a]P
- SE0002990 and SE0002991: B[a]P
- SE0002997: CO, benzene, and B[a]P

The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and corresponding predicate products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of these HPHCs in the new products as compared to their corresponding predicate products could result in increased HPHC exposures for users of the new products. The increased HPHCs include carcinogens (acetaldehyde, benzene, B[a]P), cardiovascular toxicants (benzene, CO), and reproductive and developmental toxicants (benzene, CO). Provide scientific evidence and explanation why increases in these HPHCs in the smoke of the new products, as compared to their corresponding predicate products, do not cause the new products to raise different questions of public health.

2. All of your SE Reports identify the following ingredients as being added or increased in the new products as compared to the corresponding predicate products:

[redacted]

Some of these ingredients have been associated with adverse respiratory tract effects following inhalation exposures; by using the new products in these SE Reports, consumers may be exposed to these ingredients through inhalation. The justifications by [redacted] have been considered but found inadequately supported by the information provided in the SE Reports. For example, no specific discussion is provided to explain the relevance and applicability of the information in the referenced studies to the specific differences in characteristics between the new and predicate products in the SE Reports. In addition, tobacco products do not meet the definition of food provided in 21 U.S.C. 201(f), the Federal Food, Drugs and Cosmetic Act and GRAS information is based on oral exposure data, whereas exposure to cigarette smoke is through inhalation. Further, the referenced studies usually tested a battery of constituents in combination rather than testing each component independently, and these combinations were not the same as the combinations used in the new and predicate products in the SE Reports. Provide scientific evidence to explain why the additions or

increases of these ingredients do not cause the new products 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 a toxicology perspective.

5. ENVIRONMENTAL DECISION

Under 21 CFR 25.35(b), issuance of an order finding a tobacco product Not Substantially Equivalent (NSE) under section 910(a) of the FD&C Act is categorically excluded and, therefore, normally does not require the preparation of an environmental assessment (EA) or 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 corresponding predicate tobacco products:

- Numerous changes in non-tobacco ingredients
- Changes in tobacco blend
- Changes in product design features

The applicant has failed to demonstrate that these differences in characteristics do not cause the new tobacco products to raise different questions of public health. The applicant did not provide information to uniquely identify the non-tobacco ingredients, tobacco blend, and product design features in the new and corresponding predicate tobacco products. Without this information, the composition of new and corresponding predicate products cannot be fully characterized for SE determination. Further, the applicant provided HPHC data through the testing of a remanufactured predicate, however, the applicant did not provide sufficient information on the remanufactured predicates. For instance, the applicant could have submitted a statement indicating whether all characteristics for the remanufactured predicate product (e.g. filter ventilation, porosity, tobacco, non-tobacco ingredients), and components and parts are identical. As a result, FDA could not conclude that HPHC information derived from the remanufactured predicates can stand in for information from the predicate product. In addition, although the applicant provides HPHC yields in mainstream smoke under ISO and CI smoking regimens for the new and remanufactured predicate products, there is insufficient information to determine whether the testing laboratory is considered acceptable. More specifically, complete datasets, number of replicates, standard deviations, quantitative test protocols, and storage conditions are not provided to make a scientific comparison between the measured HPHC yields between the new and predicate tobacco products. Thus, even assuming the applicant had provided sufficient information on the remanufactured predicate products, the applicant did not provide adequate method information to fully evaluate the validity of the HPHC data provided. While the applicant provided remanufactured predicate products, the applicant has failed to provide information on the remanufactured predicate products to demonstrate that they reflect the grandfathered predicate products at the time of original

manufacture. As a result, FDA cannot perform a complete evaluation to determine whether there are differences between the new and corresponding predicate product that may cause the new products to raise different questions of public health. Therefore, the applicant has failed to provide sufficient information to support a finding of substantial equivalence.

The predicate tobacco products meet statutory requirements because 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 chemistry, engineering, and toxicology 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. I concur with these reviews and recommend that NSE order letters be issued.

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

A NSE order letter should be issued for the new tobacco products in SE0002985 - SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997, as identified on the cover page of this review. The NSE order letter should cite the following deficiencies:

1. All of your SE Reports provide information about the tobacco and ingredients added to the tobacco in the new and predicate products, but limited information on the grades was provided. The information provided for the tobacco did not include sufficient detail to fully identify the composition of the new and predicate products. For example, we are unable to understand the meaning of the tobacco grades: (b) (4)(b) (4)(b) (4)(b) (4)(b) (4) (b) (4)(b) (4)(b) (4). Furthermore, (b) (4) listed twice for the(b) (4) (b) (4) for the new product. It is not clear why one grade is listed twice within the same type of tobacco. We needed additional information that uniquely identifies the tobacco used in the new and predicate products to understand the composition of the tobacco and other ingredients used in the new and predicate products. You did not provide a detailed list uniquely identifying information for all non-tobacco ingredients (e.g., CAS #, grade/purity, function) and for all tobacco (e.g., tobacco grading system) needed to fully characterize the new and predicate products. If composition differences exist between the new and predicate products, you would also need to provide a rationale for each difference with evidence and a scientific discussion for why the differences do not cause the new product to raise different questions of public health.

2. All of your SE Reports list mainstream smoke yields of TNCO and three HPHCs (acetaldehyde, benzene and B[a]P) under ISO and CI smoking regimens. However, there are discrepancies between the data sets in the GLS Report and Exhibit A of your July 10, 2017 amendment. For example, in the GLS report, the nicotine level in mainstream smoke under the ISO and CI regimen is different than what is reported in Exhibit A. Explain the data discrepancies in your amendment and identify the correct data sets for FDA to determine

whether the differences in HPHC yields do not cause the new products to raise different questions of public health.

3. All of your SE Reports contain some quantities of ingredients that require additional explanation. For example, the values of (b) (4)(b) (4)(b) (4)(b) (4)(b) (4) in seam adhesive are reported as (b) (4) mg/cigarette and 2.0 – 4.8 mg/cigarette for the new and predicate products, respectively, and the quantities of (b) (4)(b) (4)(b) (4)(b) (4) (b) (4) tipping adhesive are (b) (4) mg/cigarette for the new product. In addition, some quantities of ingredients are presented as shaded cells in the Excel sheets. The significance of the shaded cells is not evident. You needed to provide justification for reporting range quantities for these ingredients as well as the significance of the shaded cells.

4. All of your SE Report provide (b) (4) information in the ingredient list of (b) (4) (b) (4) in the Excel spreadsheets in the amendment dated March 26, 2015; however, the ingredient appears twice with two different concentrations in the same list. You needed to explain the purpose of listing the ingredient twice and identify the correct concentration.

5. All of your SE Reports compared the HPHC data of the "present day predicate" to that of the new product. You state that the "present day predicate" was constructed with the same materials and components as all of the Smokin Joes product marketed on February 15, 2007. However, you did not submit documentation demonstrating that the remanufactured predicate product at present day reflects the grandfathered predicate product at the time of the original manufacture including a side by side comparison of the ingredients, tobacco blends, and product design parameters. You needed to confirm whether there are any differences between the "present day predicate" and grandfathered predicate product. If differences exist in the product composition and design parameters between the "present day predicate" and grandfathered predicate products, you would need to provide detailed information of the differences for FDA to determine whether the "present day predicate" are reflective of the grandfathered predicate product. For example, if there is a difference in tobacco grade, provide information on the tobacco grades and grading system.

6. All of your SE Reports include data comparing the quantities of HPHCs in the new and remanufactured predicate products. However, your SE Report lacks detailed information of methods (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4), which is necessary to fully evaluate the data. You needed to provide the following information about the HPHC testing so that we can fully evaluate the HPHC data:

    a. Reference product datasets (e.g., 1R6F)
    b. Quantitative test protocols and method used
    c. A summary of the results for all testing performed

7. All of your SE Reports list ingredient quantities as percentages for casings, top flavors, plug wraps, cold glue, hot melt, printing materials, and blue monogram ink but do not specify the original units of the numerator and denominator, or define the denominator (e.g., per cigarette, per gram). In order for FDA to fully understand the composition of the new and

predicate products and make a determination of substantial equivalence, you needed to provide ingredient quantities as mass per unit of use (e.g., mg/cigarette).

8. All of your SE Reports provide information on the design parameters for the new and predicate products. However, your SE Report does not include all of the design parameters needed to fully characterize the new and predicate products. In order to adequately characterize the products, key design parameters need to be compared. Therefore, you needed to provide the actual (not approximate) target specification and upper and lower range limits for *all* of the following cigarette design parameters for the new and predicate products, as indicated:

    a. Tobacco moisture (%)
    b. Filter pressure drop (mm H_20)
    c. Filter ventilation (%)
    d. Cigarette draw resistance (mm H_2O)
    e. Filter denier per filament (DPF)
    f. Filter total denier (g/9000 m)
    g. Filter length (mm) [target specification for new product of SE0002988 only and range limits for all the new and predicate products]

    In addition, you needed to provide the upper and lower range limits for *all* of the following cigarette design parameters for the new and predicate products, as indicated:

    h. Cigarette paper band porosity (CU) [new product only]
    i. Cigarette diameter (mm) [predicate product only]

    For each of the above parameters, you needed to provide the necessary data on a per unit of product basis (e.g., filter length should be reported in mm per cigarette). If a design parameter is not applicable (e.g., band porosity if the cigarette paper does not contain bands), you needed to state as such and provide a scientific rationale.

    If a difference exists between the new and predicate products, you would need to provide a rationale for each difference in the target specification and range limits with evidence and a scientific discussion for why the difference does not cause the new product to raise different questions of public health.

9. All of your SE Reports include design parameter specifications but do not include data confirming that specifications are met. You needed to provide the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for *all* of the following cigarette design parameters for the new and predicate product unless otherwise indicated:

    a. Puff count
    b. Cigarette draw resistance (mm H_2O)
    c. Tobacco filler mass (mg)
    d. Tobacco moisture (%)
    e. Cigarette paper base paper basis weight (g/m^2)
    f. Cigarette paper base paper porosity (CU)

g. Cigarette paper band porosity (CU)
h. Denier per filament (DPF)
i. Total denier (g/9000m)
j. Filter ventilation (%)
k. Filter density (g/cm^3)
l. Filter pressure drop (mm H_2O)

For each of the above parameters, you needed to provide the data on a per unit of product basis (e.g., filter pressure drop should be reported in mm per cigarette). If a design parameter is not applicable (e.g., band porosity if the cigarette paper does not contain bands), you needed to state as such and provide a scientific rationale.

Certificates of analysis from the material supplier may have satisfied this issue. If you chose to address this issue by providing certificates of analysis for any of the parameters listed above, the certificates of analysis needed to include a target specification; quantitative acceptance criteria; parameter units; test data average value; and either the standard deviation of the test data or the minimum and maximum values of the test data. Additionally, for the design parameters listed above that were tested according to national or international standards, you needed to identify the standards and state what deviations, if any, from the standards occurred.

10. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 indicate that you may employ the use of multiple materials for cigarette paper for material supply security. However, it is unclear whether you use multiple materials for cigarette base paper, filter tow, plug wrap, tipping paper, inks, and seam adhesives for the new and predicate products, based on the material ingredients information provided in your SE Report. You needed to clarify the materials for which multiple interchangeable materials are used in the new and predicate products. In accordance with section 910(a)(1)(B) of the FD&C Act, each product modification, including use of an alternate material, constitutes a new tobacco product. A material is an alternate material if, for example, it has any difference in composition (e.g., ingredients, additives, and biological organisms). Each identified new and predicate product must consist of a single combination of cigarette base paper, filter tow, plug wrap, tipping paper, inks, and seam adhesive materials. Based on the components which you confirm employ the use of multiple interchangeable materials, you needed to identify the following:

    a. Every unique material combination in the predicate product that you are comparing to the new product.
    b. Every unique material combination in the new tobacco product. Each specific combination of materials will be considered a single new tobacco product and evaluated individually.

    You needed to provide the list of ingredients and ingredient quantities for each identified material in each new and predicate product. Additionally, you needed to provide the target specifications and upper and lower range limits for *all* of the following design parameters for each material in the new and predicate products:

    c. Cigarette base paper basis weight

d. Cigarette base paper porosity
e. Cigarette draw resistance

You also needed to provide the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for *all* of the following design parameters for each material in the new and predicate products:

f. Cigarette base paper basis weight
g. Cigarette base paper porosity
h. Cigarette draw resistance

Certificates of analysis from the material supplier may have satisfied this issue. If you chose to address this issue by providing certificate of analysis for any of the parameters listed above, the certificate of analysis needed to include target specification; quantitative acceptance criteria; parameter units; test data average value; and either the standard deviation of the test data or the minimum and maximum values of the test data.

Refer to the Preliminary Finding letter issued by FDA on March 5, 2018, which provided instructions/options on some approaches that could be used to address this issue.

11. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 provide contradictory design parameter information between the original submission and the corresponding Excel spreadsheet of the March 26, 2015 amendment regarding the overall cigarette length, overall cigarette diameter, and filter length. This prevents the complete product characterization of the design parameters. You needed to clearly state the correct target specification for the overall cigarette length, overall cigarette diameter, and filter length.

12. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 provide inconsistent information regarding the new and predicate product cigarette paper base paper porosity. In the original submissions, you use “g” as the unit of measure for the cigarette paper base paper porosity. This is not a recognized porosity unit of measure. You needed to report the cigarette paper base paper porosity using the porosity unit of measure of CORESTA Units (CU).

13. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 provide the new product “Band Porosity (CU)/Band Diffusion (cm/s)” target specifications in the March 26, 2015 amendment using “cm/s” as the unit of measure. Based on the data label, this implies that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, you provided the new product cigarette paper band porosity using “g” as the unit of measure. This is not a recognized porosity unit of measure. You needed to report the correct cigarette paper band porosity using the unit of measure of CORESTA Units (CU).

14. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 provides the filter ventilation target specifications in the original submission as <1%. This is not an exact value and prevents the complete characterization of the new and predicate

products. Furthermore, in the March 26, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate products. It is unclear if "Tip Ventilation Rate" is intended to represent filter ventilation. You needed to clarify the use of "Tip Ventilation Rate" and, if it is intended to represent filter ventilation, and provide the exact target specifications for filter ventilation for the new and predicate products.

15. SE0002985, SE0002986, SE0002988, SE0002990, SE0002991, and SE0002993 – SE0002997 include different tipping paper length values in your March 26, 2015 amendment than, those in the original SE Report. It is unclear if the values reported in the original submission or the values reported in the amendment are the correct tipping paper lengths. Additionally, if you intended to report the tipping paper "width" as the "length" in the March 26, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the March 26, 2015 amendment and the original submission for the predicate product. You needed to provide the tipping paper length target specifications for the new and predicate products.

16. All of your SE Reports include information on the tobacco filler mass and tobacco rod density of the new and predicate products. However, you did not adequately characterize either design parameter. For the tobacco filler mass of the new product and the tobacco rod density of the predicate product, you state that the data provided is "based on data from scientific consultant's physical analysis of samples of the product." Thus, the target specifications and upper and lower range limits provided reflect a sample of the actual manufacturing outcome, rather than the target and range limits of the manufacturing process. Furthermore, the reported predicate product filler mass target specifications are approximations. An exact target specification is needed in order to accurately compare the new and predicate products and determine if the new product raises different questions of public health. You needed to provide the exact target specification and upper and lower range limits for the tobacco filler mass (mg) and tobacco rod density (g/cm_3) for the new and predicate products.

17. All of your SE Reports contain incomplete band spacing and band width information for the new product. You provide a data label which lists both design parameters; however, only one target specification and one set of upper and lower range limits is provided. It is unclear which design parameter is associated with the data. You needed to identify the target specification and upper and lower range limits for both the band spacing and band width of the new product.

18. All of your SE Reports contain inconsistent information regarding the filter design parameters. You provide denier information for the new and predicate products (labeled as "Total Denier / Denier per Filament") indicating that the total denier is (b) (4) or less, and the denier per filament is (b) (4). Because total denier is the mass of 9000 m of tow, this value is typically in the thousands. It is unclear which values are the correct denier values. You needed to clarify the discrepancy and provide the target specification and upper and lower range limits for the new and predicate products for total denier and total denier per filament.

19. All of your SE Reports include information for the filter density of the new and predicate products. However, the upper and lower range limits for the predicate products require

additional clarification as the lower range limit could not be a negative value. In addition, your March 10, 2017 Amendment states that Exhibit B- 2 provides a (b) (4) certificate of analyses (COA) but this exhibit lacks filter density information. You needed to confirm the predicate product target specifications and upper and lower range limits and report the correct value as needed, as the lower range limit cannot result in a negative value. Additionally, if a difference exists between the new and predicate product target specifications or upper and lower range limits you needed to provide justification for the difference and a scientific rationale for why the difference does not cause the new product to raise different questions of public health.

20. SE0002987, SE000298, and SE0002997 indicate that there are differences in numerous filter design parameter specifications. Some of these differences have the potential to cause the new product to raise different questions of public health, while others do not. The combination of the differences in the filter design parameters (i.e., filter denier per filament, filter density, filter pressure drop, filter length) may impact smoke constituent yields of the new product. Therefore, you needed to provide scientific evidence and rationale to demonstrate that the combination of differences to the filter design parameters do not cause the new product to raise different questions of public health. Specifically, the following differences were noted which an explication is needed to why these differences do not cause the new product to raise different questions of public health:

    a. SE0002987, SE0002988, and SE0002997: the filter pressure drop of the new product decreased 11% which also exhibit CO and nicotine levels increases. Also for SE0002988, the tar level is higher in the new product
    b. SE0002987 and SE0002997: the filter length of the new product decreased by 20% in the new products which also exhibit CO and nicotine increases
    c. SE0002987 and SE0002997: the filter pressure drop and filter length decreased in the new products which also exhibit CO and nicotine increases

21. All of your SE Reports provide average values for puff count for the new and predicate products, but do not provide test protocols or data sets for the new and predicate products for puff count. You needed to provide complete test data in order to fully characterize the new and predicate products. Additionally, you needed to provide the test protocol and data sets for puff count for the new and predicate products and scientific evidence and rationale for why any differences in the puff count does not cause the new product to raise different questions of public health.

22. SE0002985, SE0002986, SE0002987, SE0002988, SE0002990, SE0002991, and SE0002997 indicate apparent increases in the following HPHCs:

    - SE0002985 and SE0002986: CO (ISO: 15%) and B[a]P (ISO: 30%; CI: 23%)
    - SE0002987 and SE0002988: CO (ISO: 20%; CI: 42%), acetaldehyde (CI: 32%), benzene (CI: 30%), and B[a]P (ISO: 49%; CI: 32%)
    - SE0002990 and SE0002991: B[a]P (CI: 14%)
    - SE0002997: CO (ISO: 27%), benzene (CI: 10%) and B[a]P (ISO: 53%; CI: 27%)

    These apparent increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate products, such as changes in

tobacco blends, cigarette papers, adhesives, and flavor ingredients. These apparent increases in smoke yields of these HPHCs in the new product as compared to the predicate product could result in increased HPHC exposures for users of the new product. The apparent increased HPHCs include carcinogens (B[a]P), cardiovascular toxicants (CO), and reproductive and developmental toxicants (CO). You needed to provide scientific evidence that the increase in these HPHCs do not cause the new product to raise different questions of public health.

23. All of your SE Reports identify a number of ingredients such as (b) (4)(b) (4) (b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4)(b) (4) among others that are added or increased in the new product as compared to the predicate product. Some of these ingredients have been associated with adverse respiratory tract effects following inhalation exposures, consumers may be exposed to these ingredients through inhalation. The justifications by (b) (4) have been considered but found inadequately supported by the information provided. For example, no specific discussion is provided to explain the relevance and applicability of the information in the referenced studies to the specific differences in characteristics between the new and predicate products. In addition, tobacco products do not meet the definition of food provided in 21 U.S.C. 201(f), the Federal Food, Drugs and Cosmetic Act and GRAS information is based on oral exposure data, whereas exposure to cigarette smoke is through inhalation. Further, the referenced studies usually tested a battery of constituents in combination rather than testing each component independently, and these combinations were not the same as the combinations used in the new and predicate products in the SE Reports. You needed to provide scientific evidence to explain why the additions or increases of these ingredients do not cause the new products to raise different questions of public health.