Technical Project Lead (TPL) Review: SE0002153

SE0002153: Maverick Menthol Silver Box 100s	
Package Type	Box
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.89 mm
Filter Ventilation	58%
Characterizing Flavor	Menthol
Common Attributes of SE Reports	
Applicant	ITG Brands, LLC
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Filtered Combusted
Recommendation	
Issue a Not Substantially Equivalent (NSE) Order.	

Technical Project Lead (TPL):

Digitally signed by Matthew R. Holman -S
Date: 2016.07.06 07:46:00 -04'00'

Matthew R. Holman, Ph.D.
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 David Ashley -S
Date: 2016.07.06 07:58:53 -04'00'

David L. Ashley, Ph.D.
RADM (Ret.), U.S. Public Health Service
Director
Office of Science

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1. BACKGROUND

1.1. PREDICATE TOBACCO PRODUCT

The applicant submitted the following predicate tobacco product:

SE0002153	Maverick Menthol Silver Box 100s
Product Name	Kent III Ultra Lights 100s
Package Type	Soft pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	7.89 mm
Filter Ventilation	55%
Characterizing Flavor	None

The predicate tobacco product is a combusted, filtered cigarette manufactured by Lorillard[1].

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

On March 22, 2011, the applicant submitted the SE Report. FDA completed Jurisdiction Review and issued Acknowledgment letter on August 23, 2011. On October 26, 2011, the applicant submitted an Environmental Assessment. FDA issued an Advice/Information Request letter (A/I letter) on January 4, 2013. On January 31, 2013, the applicant submitted a response to the A/I letter. On February 7, 2014, the applicant submitted a response to FDA's request for additional new and predicate product information. A Notification letter was issued on May 11, 2015, indicating that scientific review was expected to begin on June 25, 2015. On June 12, 2015, during the notification period, FDA received a Notice of Merger from Lorillard (TC0001319). The notice indicated a transfer of ownership from Lorillard Tobacco Company to R.J. Reynolds and to Imperial Tobacco Group (referred to as ITG Brands). On June 23, 2015, ITG Brands attempted to submit an unsolicited amendment ((b) (4) to the SE Report; however, the submission format could not be opened and archived by the Document Control Center (DCC). On August 6 and August 7, 2015, FDA held two teleconferences with the applicant to clarify the file formats accepted by DCC. On August 10, 2015, FDA received a resubmission of the June 23, 2015, amendment, which was assigned a new submission tracking number (b) (4)). Because the June 23, 2015, amendment could not be archived, it was deactivated by the DCC and, therefore, not reviewed by FDA at that time. However, because the new amendment (b) (4)) could be archived and was confirmed by FDA as being submitted by an authorized point of contact (POC) for the SE Report, FDA reviewed this amendment. On August 26, 2015, FDA received another unsolicited amendment ((b) (4) by the authorized POC with corrections to the original SE Report and the August 10, 2015, amendment.

[1] After the transfer of ownership, the predicate tobacco product became owned by R.J. Reynolds.

On October 9, 2015, FDA acknowledged transfer of ownership for the Maverick brand products to ITG Brands.

Product Name	SE Report	Amendments
Maverick Menthol Silver Box 100s	SE0002153	(b) (4)

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 Rosanna Beltre on January 4, 2013, and by Angela Brown on March 11, 2014.

The final review concludes that the SE Report is administratively complete.

3. COMPLIANCE REVIEW

The Office of Compliance and Enforcement (OCE) completed a review to determine whether the applicant established that the predicate tobacco product is a grandfathered product (i.e., was commercially marketed as of February 15, 2007). The OCE review dated June 15, 2015, concludes that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco product is grandfathered and, therefore, is an eligible predicate tobacco product.

Because the new tobacco product is not substantially equivalent to the predicate tobacco product, OCE did not complete a review to determine whether the new tobacco product is in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), as required by section 910(a)(2)(A)(i)(II) of the FD&C Act.

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 Matthew Hassink on October 9, 2015.

The chemistry review concludes that the new tobacco product has different characteristics related to product composition compared to the predicate tobacco products and that the SE Report does not contain sufficient detail to determine that the differences with respect to product composition do not cause the new tobacco product to raise different questions of public health.[2] The review identifies the following deficiencies[3] that have *not* been adequately resolved:

1. All of your SE Reports provide information about tobacco and ingredients added to tobacco in the predicate and new products. However, your SE Reports do not include ingredients in all components of the predicate and new products, including the non-FSC cigarette paper. Without this information, we cannot determine whether the predicate and new products are substantially equivalent. We need any other information you may have that uniquely identifies the tobacco and non-tobacco ingredients used in the predicate and new products. This is the information that you rely on to ensure that the tobacco and non-tobacco ingredients used in the predicate and new products are identical for both products. For example, 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 predicate and new products. Provide a detailed list including:

    a. Ingredients for components including:
        i. Non-FSC cigarette paper
        ii. FSC cigarette paper
        iii. Tipping paper
        iv. Plug wrap
        v. Monogram ink
    b. Uniquely identifying information for all tobacco (e.g., tobacco grading system)
    c. Uniquely identifying information for ingredients (e.g., CAS #, grade/purity, function)

    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. Also, clarify the

[2] It should be noted that the chemistry review states that the (b) (4) yield causes the new tobacco product to raise different questions of public health but then states in the conclusion that there is insufficient information to determine whether the (b) (4) yield causes the new tobacco product to raise different questions of public health. The actual conclusion of the review is that there is insufficient information to determine whether the differences in characteristics (including the (b) (4) yield) cause the new tobacco product to raise different questions of public health.

[3] It should be noted the chemistry review evaluated SE Reports in addition to SE0002153, but only the deficiencies applicable to SE0002153 are captured in this TPL review.

function of (b) (4), as you listed the function of this ingredient as (b) (4).

2. (b) (4) and (b) (4) provide information on the tobacco blend of the new and predicate products. The SE Reports list (b) (4) as an ingredient in the tobacco blend in Section 7.3.1 of the reports. However, no (b) (4) is reported in the ingredient table (Table 7.3.a) of the reports for the new or predicate products. Clarify if (b) (4) is included in the new and predicate products. If (b) (4) is present, provide the quantity (i.e., mg/cig) of (b) (4) present in the new and predicate products. Additionally, provide information to uniquely identify the (b) (4) tobacco ingredient in the new and predicate products.

3. All of the SE Reports provide information on the ink used in the new and predicate products. The SE Reports state that the new products use a different monogram ink than the corresponding predicate products. However, no information regarding the ingredients of the monogram ink used in the new and predicate products is provided. In addition, table 7.3.b of the reports (b) (4) and (b) (4) lists the same ink in the new and predicate products, which seems to contradict the statement made in your reports that a different ink is used. Clarify the identity of the ink(s) used in the new and predicate products in (b) (4) and (b) (4). Different inks are reported, in (b) (4) for the new and corresponding predicate product and different inks are possibly used in the new and corresponding predicate products reported in (b) (4) and (b) (4). When different inks are used in the new and corresponding predicate products, provide the ingredients for the inks and the uniquely identifying information for all the ingredients of the inks (e.g., CAS#).

4. All of your SE Reports lack information about complex ingredients. For example, your SE Reports lack the names, functions, or quantities of the single ingredients in the flavoring mixtures (b) (4). Distinguish between complex ingredients made to your specifications and those that are not. For all complex ingredients made to your specifications, provide complete information according to FDA's Guidance for Industry Listing of Ingredients in Tobacco Products.

5. SE0002153 and (b) (4) identify flavor differences between the new and corresponding predicate products. For example, (b) (4) is only listed in the new products, whereas (b) (4) flavor is only listed in the predicate products. Such differences are expected to have an impact on smoke chemistry. Sugars are known to increase the

mainstream smoke yields of certain carbonyls and hydrocarbons, such as formaldehyde. In addition, sugars and other flavors are used in tobacco products to mitigate the harshness of cigarette smoke or to enhance the product's appeal. Provide evidence and a scientific rationale as to why such differences do not cause the new products to raise different questions of public health.

6. SE0002153 and (b) (4) provide data regarding HPHC yields for the new and predicate products. However, due to the differences between the new and corresponding predicate products, the data provided is not sufficient to perform a full evaluation of the new products. The differences between the new and predicate products include (b) (4) being present in the new products, as a tobacco ingredient, but not the corresponding predicate products. (b) (4) has been shown to increase the level of ammonia in mainstream smoke. In addition, the new products contain (b) (4) tobacco. The mainstream smoke generated from (b) (4) tobaccos has been shown to contain higher amounts of NNN and NNK than (b) (4) tobaccos, while pyrolysis of tobacco has been shown to produce CO. There are also flavor differences between the new and corresponding predicate products. These differences include higher amounts of (b) (4) and sugars. Pyrolysis of (b) (4) can result in the formation of phenol and formaldehyde, while pyrolysis of sugars can result in the formation of certain carbonyls and hydrocarbons, such as formaldehyde and acetone. These differences between the new and corresponding predicate products may cause the new products to raise different questions of public health. Provide scientific rationale and evidence to address why these differences do not cause the new products to raise different questions of public health. Your response should include addressing the (b) (4) yields for the new products under non-intense smoking regimens.

   One way to provide such data is to measure mainstream smoke yields of the following HPHCs in the predicate and new products under the Canadian Intense smoking regimen:

   a. Tar (NFDPM)
   b. Carbon monoxide
   c. Nicotine (total)

   In addition, data could also include measurement of mainstream smoke yields of the following HPHCs from the predicate products under a non-intense smoking regimen:

   d. Acetone
   e. Ammonia

f. Formaldehyde
g. NNN
h. NNK

This data for the predicate products would allow comparison to the yields of the HPHCs provided for the new products. It would also be helpful to have yields for the same HPHCs from the new and predicate products under the Canadian Intense smoking regimen. If you measure these HPHC yields, be sure to include all of the information pertinent to the analyses as you have done for the HPHC data that you have already submitted (e.g., analytical methods used, number of replicates, complete datasets).

It is an applicant's responsibility to provide appropriate scientific evidence and data for the predicate tobacco product. It is unclear if the predicate products are available for testing. If the predicate products are available, testing should be performed on the appropriate predicate products. However, if your predicate product is not available for testing, there are options which you may choose to pursue to try to demonstrate substantial equivalence. Below are some options, though other alternative options may be acceptable. For example, the predicate product can be manufactured 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, the MSS HPHC 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. Another option would be to submit MSS HPHC data for products other than the predicate and new products (referred to as surrogate tobacco products) that can be extrapolated to the predicate and new products. In this case, data for the surrogate tobacco products could be submitted in place of data for the predicate and new tobacco products; the data should demonstrate that the differences in characteristics between the predicate and new products do not cause the new tobacco product to raise different questions of public health. In order to extrapolate such data, the HPHC smoke data should be produced from surrogate tobacco products as similar as possible in characteristics to the predicate and new products. In addition to the smoke data, information comparing the surrogate tobacco products to the predicate and new products should also be submitted.

Therefore, the review concludes that there was inadequate information from a chemistry perspective to determine that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

It should be noted that the chemistry review discusses the presence of menthol in the new tobacco product and absence of menthol in the predicate product. The chemistry review does not reach a conclusion about the presence of menthol. Rather, it defers to the addiction review to evaluate this issue.
It should also be noted that Deficiency 1 and 3 both require unique identification of monogram inks (e.g., CAS #). This information only needs to be conveyed to the applicant in a single deficiency in the order letter.

4.2. ENGINEERING

An engineering review was completed by Komal Ahuja on October 6, 2015.

The engineering review concludes that the new tobacco product has different characteristics related to product design compared to the predicate tobacco product and that the SE Report does not contain sufficient detail to determine that the differences with respect to product engineering do not cause the new tobacco product to raise different questions of public health. The review identifies the following deficiencies[4] that have *not* been adequately resolved:

1. All of your SE Reports provide information on the design parameters for the predicate and new products. You include the target specifications and upper and lower range limits for some but not all of the design parameters. In order to adequately characterize the products, it is necessary to compare key design parameters. Provide the **target specifications** for *all* of the following cigarette design parameters for each predicate and new product, unless otherwise noted:

    a. Cigarette draw resistance (mm H_2O);
    b. Filter efficiency (%) [If no filter efficiency data is available for the products, include information sufficient to show that the cigarette filter is unchanged (e.g., denier per filament, total denier, and filter density)].

    Provide the **upper and lower range limits** for *all* of the following cigarette design parameters for each predicate and new product, unless otherwise noted:

    c. Cigarette circumference (mm) (predicate products only);
    d. Cigarette draw resistance (mm H_2O);
    e. Cigarette paper base paper basis weight (g/m^2);
    f. Cigarette paper base paper porosity (CU);
    g. Cigarette paper band porosity (CU) (new products only);
    h. Cigarette paper band width (mm) (new products only);
    i. Cigarette paper band space (mm) (new products only); and

[4] It should be noted the engineering review evaluated SE Reports in addition to SE0002153, but only the deficiencies applicable to SE0002153 are captured in this TPL review.

j. Filter efficiency (%) [If no filter efficiency data is available for the products, include information sufficient to show that the cigarette filter is unchanged (e.g., denier per filament, total denier, and filter density)].

For each of the above parameters, provide the necessary data on a per unit of product basis (e.g., tipping paper 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.

2. All of your SE Reports include design parameter specifications but do not include data confirming that specifications are met. 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 predicate and new products, unless otherwise noted:

   a. Cigarette draw resistance (mm H_2O);
   b. Tobacco filler mass (mg);
   c. Cigarette paper base paper basis weight (g/m^2);
   d. Cigarette paper base paper porosity (CU); and
   e. Cigarette paper band porosity (CU) (new products only).

   For each of the above parameters, provide the necessary data on a per unit 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 and provide a scientific rationale.

   Certificates of analysis from the material supplier may satisfy this deficiency. If you choose to address this deficiency by providing certificates of analysis for any of the parameters listed above, the certificates of analysis 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.

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.

If you choose to provide filter efficiency in place of filter density, denier per filament, and total denier, provide test data as described above for filter efficiency.

3. SE0002153 and (b) (4) indicate differences in design parameters that need additional information in order to adequately characterize the products. The target specifications for (b) (4) from the predicate to new products. You provide a limited rationale for these differences without a discussion of the impact on public health. An (b) (4) may increase smoke constituents. Therefore, provide a rationale with evidence and a scientific discussion of why the (b) (4) differences do not cause the new products to raise different questions of public health.

4. All of your SE Reports include design parameter specifications but do not include all of the necessary data confirming that specifications are met. Provide the information below for the following cigarette design parameters for each predicate and new product:

    a. You provide puff count test data. However, the predicate and new products were measured under two different smoking regimens without a method to link the two regimens together and in turn cannot be accurately compared. Either provide the puff count data under the same smoking regimen or illustrate how the two methods can be compared quantitatively. 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.
    b. You submitted the calculated filter efficiency data from the smoke analysis testing. However, test data is a factor in characterizing the product and is used to evaluate if specifications are met; therefore, test data needs to be based on actual results and not theoretical values. Provide test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results, from the manufacturing process for filter efficiency. Additionally, without submitting criteria to verify the data against, the test data does not prove useful. Therefore, provide the corresponding target specifications and range limits in order to evaluate the test data. In lieu of filter efficiency, you may submit target specifications, range

limits, and test data for total denier, denier per filament, and filter density.

5. All of your SE Reports provide test data for cigarette design parameters that do not fall within your upper and lower range limits for the new and predicate products, indicating the specifications are not met. Therefore, confirm these values and justify the following discrepancies:

   a. In (b) (4) (new product only), (b) (4), SE0002153 (predicate product only), (b) (4) (predicate product only), and (b) (4) (predicate product only), some of the tobacco oven volatiles data points do not fall within the respective range limits for the predicate and/or new products.
   b. In (b) (4), SE0002153, (b) (4) (predicate product only), (b) (4), some of the filter pressure drop data points do not fall within the respective range limits for the predicate and/or new products.
   c. In (b) (4), SE0002153, (b) (4) (predicate product only), (b) (4) (new product only), (b) (4), and (b) (4), some of the filter ventilation data points do not fall within the respective range limits for the predicate and/or new products.

Therefore, the review concludes that there was inadequate information from an engineering perspective to determine that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

It should be noted that Deficiency 1 requests information demonstrating the relationship between puff count determined by two different smoking regimens. However, the chemistry review concludes that (b) (4) ." This same conclusion can be drawn about puff count. Using this correlation between the two smoking regimens, the submitted puff count data does not cause the new tobacco product to raise different questions of public health. Therefore, part a of Deficiency 1 does not need to be conveyed to the applicant in the order letter.

4.3. TOXICOLOGY

A toxicology review was completed by Lynn Crosby on November 23, 2015.

The toxicology review concludes that the new tobacco product has different characteristics related to product toxicity compared to the predicate tobacco product and that the SE Report does not contain sufficient detail to determine

that the differences with respect to product toxicology do not cause the new tobacco product 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 indicate that the new products contain ingredients or complex ingredients that can form HPHCs during pyrolysis, while the predicate products do not contain these ingredients. In addition, your SE Reports did not provide the levels of some of these ingredients in the predicate products. For all SE Reports, provide ingredient information for both the predicate and new products components, sub-components, and complex ingredients listed below:

    - (b) (4) : (b) (4) , predicate cigarette paper, LIP cigarette paper, LIP base paper, ink, plug wrap, tipping paper, (b) (4)
    - (b) (4) : predicate cigarette paper, LIP cigarette paper, LIP base paper, ink, plug wrap, tipping paper, (b) (4)
    - (b) (4) : blend changes, (b) (4) predicate cigarette paper, LIP cigarette paper, LIP base paper, ink, plug wrap, tipping paper, (b) (4)
    - (b) (4) : blend changes, (b) (4) predicate cigarette paper, LIP cigarette paper, LIP base paper, ink, plug wrap, tipping paper, (b) (4)
    - (b) (4) (b) (4) predicate cigarette paper, LIP cigarette paper, Alternate LIP cigarette paper, LIP base paper, ink, plug wrap, tipping paper, (b) (4)
    - (b) (4) : (b) (4) predicate cigarette paper, LIP cigarette paper, LIP base paper, ink, plug wrap,

[5] It should be noted the toxicology review evaluated SE Reports in addition to SE0002153, but only the deficiencies applicable to SE0002153 are captured in this TPL review.

tipping paper, (b) (4)

- (b) (4) :(b) (4) , predicate cigarette paper, LIP cigarette paper, LIP base paper, Alternate LIP cigarette paper, ink, plug wrap, tipping paper, (b) (4)

Address the potential impact that any of these ingredient changes may have on HPHC deliveries in the new products as compared to the predicate products. Document the major chemical components that the complex ingredients contain, especially those which have pharmacological or toxicological properties. Provide evidence (data, peer reviewed articles or other scientifically robust data sources, including information relevant to the inhalation route) that the addition of these ingredients, their combustion products, or their effects on the combustion of the new product do not cause the new products to raise different questions of public health.

Therefore, the review concludes that there was inadequate information from a toxicology perspective to determine that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health. It should be noted that the toxicology review also concluded that numerous deficiencies identified in the chemistry review are also applicable to the toxicology review.

4.4. ADDICTION

A behavioral pharmacology review[6] was completed by Olga Rass on October 19, 2015.

The behavioral pharmacology review concludes that the new tobacco product has different characteristics compared to the predicate tobacco product and that the addition of menthol causes the new tobacco product to raise different questions of public health[7] and that the SE Report does not contain sufficient detail to determine that the other differences with respect to consumer use of the product and its impact on behavior do not cause the new tobacco product to raise

[6] Because the new and predicate products have broadly similar product formats, behavioral factors (e.g., use characteristics) are likely to be the primary determinants of exposure-response characteristics and harm. Therefore, a behavioral pharmacology review was completed, but a clinical pharmacology review was not.

[7] It should be noted that the behavioral pharmacology review states that the addition of menthol to a non-mentholated product *may* cause the new tobacco product to raise different questions of public health but then states elsewhere that "[t]he addition of menthol to the new product raises different questions of public health." The actual conclusion of the review is that the addition of menthol does cause the new tobacco product to raise different questions of public health.

different questions of public health. The review identifies the following deficiencies that have *not* been adequately resolved:

1. Your SE Report includes information on the menthol content of the new product. The new product is mentholated while the predicate product is not. You claim that the addition of menthol does not raise different questions of public health. However, the addition of menthol may impact the flavor and sensory effects of the new product and affect use behavior. Mentholated tobacco products may impact initiation behaviors and progression to regular tobacco use by increasing palatability and abuse liability, increasing levels/severity of dependence, and reducing the likelihood of cessation. The addition of menthol to the new product raises different questions of public health.

2. Your SE Report includes information on changes in sweeteners and other flavors in the new product. You claim that the differences in sweeteners and other flavors do not raise different questions of public health. However, the addition and increased amounts of sweeteners and flavors/flavor enhancers may impact the tobacco flavor of the new product and affect use behaviors. The sweeteners and flavors in the new product may be attractive to youth and inexperienced users and impact initiation behaviors and progression to regular tobacco use by increasing palatability and abuse liability. Provide scientific data and rationale demonstrating that the changes in sweeteners do not cause the new product to raise different questions of public health. This may include the results from properly-designed taste panels comparing the new product and predicate product or a clinical abuse liability assessment comparing the new product and predicate product. There may be other ways of satisfying this deficiency and you are responsible for identifying how best to do this.

Therefore, the review concludes that, from a behavioral pharmacology perspective, the addition of menthol causes the new tobacco product to raise different questions of public health and that there was inadequate information to determine that the other differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

5. ENVIRONMENTAL DECISION

A finding of no significant impact (FONSI) was signed by RADM David L. Ashley on November 19, 2013. The FONSI was supported by an environmental assessment prepared by FDA on November 14, 2013.

6. CONCLUSION AND RECOMMENDATION

The following is the key difference in characteristics between the new and predicate tobacco products:

- Addition of menthol

The new tobacco product does not meet the statutory requirements for a determination of substantial equivalence. It is possible that the applicant could resolve the deficiencies identified in the chemistry, engineering, and toxicology reviews. In other words, these reviews conclude that there was inadequate information to determine that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health. However, the behavioral pharmacology review concludes that the addition of menthol in the new tobacco product causes it to raise different questions of public health because menthol may impact initiation behaviors and progression to regular tobacco use by increasing palatability and abuse liability, increasing levels/severity of dependence, and reducing the likelihood of cessation. I agree with the conclusion of the behavioral pharmacology review that the addition of menthol causes the new tobacco product to raise different questions of public health.

Based on this conclusion, neither an Advice/Information Request nor a Preliminary Finding letter is appropriate for this SE Report. These letters are issued to allow applicants to respond to deficiencies so that they may have the opportunity to demonstrate that the differences in characteristics between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health. Neither an Advice/Information nor a Preliminary Finding letter is warranted for this SE Report because the applicant cannot demonstrate a different conclusion for its new tobacco product in light of the currently available evidence and data. Instead, I recommend that an NSE order letter be issued.

The predicate tobacco product meets statutory requirements because it is a grandfathered product (i.e., was commercially marketed in the United States as of February 15, 2007).

FDA examined the environmental effects of finding the new tobacco product not substantially equivalent and made a finding of no significant impact.

An NSE order letter should be issued for the new tobacco product in SE0002153, as identified on the cover page of this review. The NSE order letter should cite the following key deficiency:

1. Your SE Report indicates that the new tobacco product is mentholated but the predicate tobacco product is not. You claim that the addition of menthol does not cause the new tobacco product to raise different questions of public health. However, the addition of menthol may impact the flavor and sensory effects of the new tobacco product and affect use behavior. The addition of

menthol causes the new tobacco product to raise different questions of public health because menthol likely impacts initiation behaviors and progression to regular tobacco use by increasing palatability and abuse liability, increasing levels/severity of dependence, and reducing the likelihood of cessation.

In addition to this deficiency demonstrating that the new tobacco product is not substantially equivalent to the predicate tobacco product, the NSE order letter should list the following deficiencies that prevent a determination of substantial equivalence:

2. Your SE Report provides information about tobacco and ingredients added to tobacco in the new and predicate tobacco products. However, your SE Report does not include ingredients in the following components of the new and predicate tobacco products:

    a. Cigarette paper
    b. Tipping paper
    c. Plug wrap
    d. Monogram ink

    In addition, your SE Report does not include information needed to uniquely identify tobacco (e.g., tobacco grading system) and non-tobacco ingredients (e.g., CAS #, grade/purity, function). The function of (b) (4) needs clarification, as your SE Report lists the function of this ingredient as both a (b) (4). If differences exist between the composition of the new and predicate tobacco products, scientific discussion for why the differences do not cause the new tobacco product to raise different questions of public health would be needed.

3. Your SE Report provides information on the tobacco blend of the new and predicate tobacco products. Your SE Report lists (b) (4) as an ingredient in the tobacco blend in Section 7.3.1. However, no (b) (4) is reported in the ingredient table in Table 7.3.a. Therefore, clarification is needed on whether (b) (4) is included in the new and predicate tobacco products. If (b) (4) is present, the quantity (in mg/cig) is needed along with information needed to uniquely identify (b) (4) in the new and predicate tobacco products.

4. Your SE Report provides information on the ink used in the new and predicate tobacco products and states that different ink is used in the new and predicate tobacco products. However, no information is provided regarding the ingredients of the monogram ink used in the new and predicate tobacco products. In addition, Table 7.3.b lists the same ink in the new and predicate tobacco products, which seems to contradict the statement made in the SE Report that a different ink is used. Therefore, clarification on the

identity of the monogram ink used in the new and predicate tobacco products is needed.

5. Your SE Report lacks adequate information on the composition of the complex ingredients. Distinguish between complex ingredients made to your specifications and those that are not. For all complex ingredients made to your specifications, your SE Report needs to list the names, functions, and quantities of the single ingredients that comprise the complex ingredients.

6. Your SE Report identifies flavor differences between the new and predicate tobacco products. For example, (b) (4) is listed in the new tobacco product, whereas (b) (4) flavor is listed in the predicate tobacco product. Such differences may impact smoke chemistry, as sugars are known to increase the mainstream smoke yields of certain carbonyls and hydrocarbons, such as formaldehyde. In addition, sugars and other flavors are used in tobacco products to mitigate the harshness of cigarette smoke and to enhance product appeal. Scientific evidence as to why such differences do not cause the new tobacco product to raise different questions of public health is needed.

7. Your SE Report indicates significant differences in the tobacco blends of the new and predicate tobacco products. The new tobacco product contains (b) (4) tobacco than the predicate tobacco product. The mainstream smoke generated from (b) (4) tobacco has been shown to contain higher amounts of NNN and NNK than from (b) (4) tobacco. In addition, (b) (4) (b) (4) is present in the new tobacco product but not the predicate tobacco product. (b) (4) has been shown to increase the level of ammonia in mainstream smoke. There are also flavor differences between the new and predicate tobacco products, including higher amounts of (b) (4) and sugars. Pyrolysis of (b) (4) can result in the formation of phenol and formaldehyde, while pyrolysis of sugars can result in the formation of certain carbonyls and hydrocarbons, such as formaldehyde and acetone. Scientific rationale and evidence to address why these differences do not cause the new tobacco product to raise different questions of public health. One way to provide such evidence is to measure mainstream smoke yields of the following HPHCs in the new and predicate tobacco products under the Canadian Intense smoking regimen:

    a. Tar
    b. Carbon monoxide
    c. Nicotine

Such evidence could include measurement of mainstream smoke yields of the following HPHCs in the predicate tobacco products under the ISO smoking regimen:

d. Acetone
e. Ammonia
f. Formaldehyde
g. NNN
h. NNK

8. Your SE Report provides information on the design parameters for the new and predicate tobacco products. You include the target specifications and upper and lower range limits for some but not all of the design parameters. **Target specifications** for *all* of the following design parameters for the new and predicate tobacco products are not provided and are needed to adequately characterize the products:

   a. Cigarette draw resistance (mm H_2O)
   b. Filter efficiency (%) [If no filter efficiency data is available for the products, include information sufficient to show that the cigarette filter is unchanged (e.g., denier per filament, total denier, and filter density)]

   In addition, the **upper and lower range limits** for *all* of the following design parameters for the new and predicate tobacco products are not provided and are needed to adequately characterize the products:

   c. Cigarette circumference (mm) (predicate tobacco product only)
   d. Cigarette draw resistance (mm H_2O)
   e. Cigarette paper base paper basis weight (g/m^2)
   f. Cigarette paper base paper porosity (CU)
   g. Cigarette paper band porosity (CU) (new tobacco product)
   h. Cigarette paper band width (mm) (new tobacco product)
   i. Cigarette paper band space (mm) (new tobacco product)
   j. Filter efficiency (%) [If no filter efficiency data is available for the products, include information sufficient to show that the cigarette filter is unchanged (e.g., denier per filament, total denier, and filter density)]

   If differences in target specifications or range limits exist between the new and predicate tobacco products, scientific evidence and discussion would be needed to demonstrate why the differences do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report includes design parameter specifications but does not include data confirming that specifications are met. **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 the new and predicate tobacco products are not provided and are needed to adequately characterize the products:

a. Cigarette draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Cigarette paper base paper basis weight (g/m^2)
d. Cigarette paper base paper porosity (CU)
e. Cigarette paper band porosity (CU) (new tobacco product only)

Certificates of analysis from the material supplier may satisfy this deficiency.

10. Your SE Report indicates differences in design parameters that need additional information in order to adequately characterize the products. The target specifications for (b) (4) from the predicate to new tobacco product. Your SE Report provides a limited rationale for these differences without a discussion of the impact on public health. An (b) (4) may increase smoke constituents. Therefore, scientific evidence and discussion of why the (b) (4) differences do not cause the new tobacco product to raise different questions of public health is needed.

11. Your SE Report includes design parameter specifications but does not include all of the necessary data confirming that specifications are met. Your SE Report provides filter efficiency calculated from smoke analysis. However, test data is a factor in characterizing the product and is used to evaluate if specifications are met; therefore, test data needs to be based on actual results and not theoretical values. Additionally, without submitting criteria to verify the data against, the test data is of limited utility.

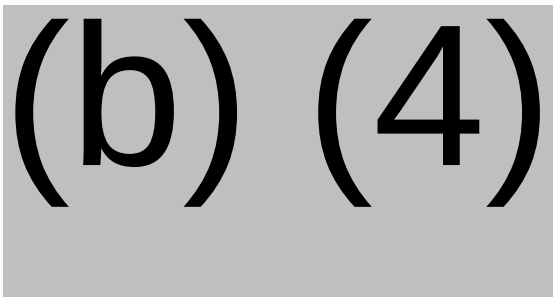
12. Your SE Report provides test data for design parameters that do not fall within your upper and lower range limits for the new and predicate tobacco products, indicating the specifications are not met. Therefore, confirmation of the range limits is needed along with justification for the discrepancies:

a. Tobacco oven volatiles (predicate tobacco product only)
b. Filter pressure drop
c. Filter ventilation

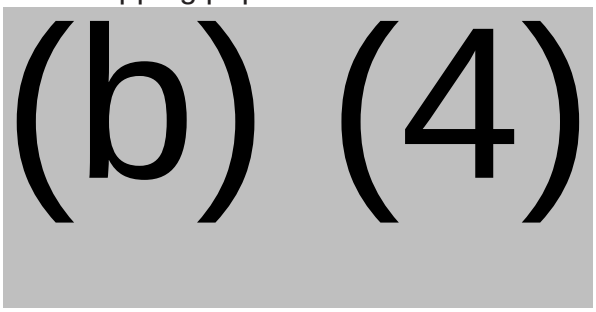
13. Your SE Report indicates that the new tobacco product contains ingredients that can form HPHCs during pyrolysis, while the predicate tobacco product does not contain these ingredients. In addition, your SE Report does not provide the quantities of these ingredients in the predicate tobacco product. Ingredient information, including components, sub-components, and single

ingredients comprising complex ingredients, is needed for the following ingredients in the new and predicate tobacco products:

a. Tobacco blend



j. Cigarette paper
k. Ink
l. Plug wrap
m. Tipping paper



Scientific evidence and discussion is needed to demonstrate that differences in ingredients between new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health, addressing the impact of these differences on smoke toxicity.

14. Your SE Report includes information on changes in sweeteners and other flavors in the new tobacco product. You claim that the differences in sweeteners and other flavors do not cause the new tobacco product to raise different questions of public health. However, the addition and increased amounts of sweeteners and flavors/flavor enhancers may impact the tobacco flavor of the new tobacco product and affect use behaviors. The sweeteners and flavors in the new tobacco product may be attractive to youth and inexperienced users and impact initiation behaviors and progression to regular tobacco use by increasing palatability and abuse liability. However, your SE Report does not provide scientific data and rationale demonstrating that the changes in sweeteners do not cause the new tobacco product to raise different questions of public health. Such evidence could include properly-designed taste panels comparing the new and predicate tobacco products or a clinical abuse liability assessment comparing the new and predicate tobacco products.