FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review:

SE0003026, SE0003027, SE0003028, SE0003029, SE0003030, SE0003031, and SE0003032

SE0003026: Smokin Joes Natural Silver 100 Size Box Fire Safe	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None
SE0003027: Smokin Joes Natural Silver 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None
SE0003028: Smokin Joes Natural Silver King Size Box Fire Safe	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.8 mm
Ventilation	None
Characterizing Flavor	None
SE0003029: Smokin Joes Natural Silver King Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None
SE0003030: Smokin Joes Natural White 100 Size Box Fire Safe	
Package Type	Hard Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None

SE0003031: Smokin Joes Natural White 100 Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	99 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None
SE0003032: Smokin Joes Natural White King Size Soft Pack Fire Safe	
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	Not Provided
Ventilation	None
Characterizing Flavor	None
Common Attributes of SE Reports	
Applicant	Smokin Joes
Report Type	Provisional
Product Category	Cigarette
Product Sub-Category	Combusted Filtered
Recommendation	
Issue Not Substantially Equivalent (NSE) orders.	

Technical Project Lead (TPL):

Todd L. Cecil -S
Digitally signed by Todd L. Cecil -S
Date: 2018.06.26 10:02:12 -04'00'

Todd Cecil, Ph.D.
Associate Director
Division of Product Science

Signatory Decision:

☒ Concur with TPL recommendation and basis of recommendation

☐ Concur with TPL recommendation with additional comments (see separate memo)

☐ Do not concur with TPL recommendation (see separate memo)

Digitally signed by Matthew R. Holman -S
Date: 2018.07.05 07:29:25 -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:

SE0003026: Smokin Joes Natural Silver 100 Size Box Fire Safe	
Product Name	Smokin Joes Natural Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	Not Provided[1]
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None
SE0003027: Smokin Joes Natural Silver 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Natural Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	Not Provided[1]
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None
SE0003028: Smokin Joes Natural Silver King Size Box Fire Safe	
Product Name	Smokin Joes Natural Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None
SE0003029: Smokin Joes Natural Silver King Size Soft Pack Fire Safe	
Product Name	Smokin Joes Natural Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None

[1] During scientific review, the applicant provided inconsistent target specifications regarding predicate product length. Therefore, FDA could not evaluate it.

SE0003030: Smokin Joes Natural White 100 Size Box Fire Safe	
Product Name	Smokin Joes Natural Ultra Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	Not Provided[1]
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None
SE0003031: Smokin Joes Natural White 100 Size Soft Pack Fire Safe	
Product Name	Smokin Joes Natural Ultra Light 100's Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	Not Provided[1]
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None
SE0003032: Smokin Joes Natural White King Size Soft Pack Fire Safe	
Product Name	Smokin Joes Natural Ultra Light King Soft Pack
Package Type	Soft Pack
Package Quantity	20 cigarettes
Length	84 mm
Diameter	7.91 mm
Ventilation	None
Characterizing Flavor	None

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

1.2. REGULATORY ACTIVITY RELATED TO THIS REVIEW

FDA received the seven provisional SE Reports listed above on March 22, 2011 from Joseph Anderson d/b/a Smokin Joes (Smokin Joes). FDA issued Acknowledgement letters on August 31, 2011. On June 8, 2012, FDA received the applicant's amendment in response to FDA's June 4, 2012 information request via telecon to clarify the names of the new tobacco products (SE0004569). On December 28, 2012, FDA issued Advice/Information (A/I) Request letters for these SE Reports. On January 18, 2013, FDA received a request for an extension of time, until February 28, 2013 to respond to the December 28, 2012 A/I Request letters (SE0006310). FDA responded to the applicant's request for extension of time on January 31, 2013, by calling the applicant and informing them that their response to the December 28, 2012 A/I Request letters would not be due on January 29, 2013 and that FDA

would be sending a letter with further instructions.[2] On February 28, 2013, FDA received Smokin Joes' responses (SE0007587-SE0007593) to the December 28, 2012 A/I Request letters.

On March 4, 2013, FDA emailed Smokin Joes to requesting further information for unique identification of the new and predicate products, namely "short version" of the tobacco product names, "full version" of the tobacco product names, package type, and the number of cigarettes in each package. On March 19, 2013, FDA received the applicant's amendment in response to our March 4, 2013 information request (SE0009117). On July 9, 2013, FDA issued a Correction letter informing Smokin Joes that FDA had revised its records to include clarifications to the new tobacco product names. On July 31, 2013, Smokin Joes' wrote to FDA in response to FDA's July 9, 2013 Correction letter and several e-mails from FDA/CTP's Office of Compliance and Enforcement regarding clarification of the predicate/grandfathered tobacco product names (SE0009439). In response to the former, Smokin Joes provided further edits to the product names contained in FDA's July 9, 2013 letter.

FDA issued a Notification letter on May 11, 2015, informing Smokin Joes that scientific review of these SE Reports would begin on June 25, 2015. On June 24, 2015, FDA received a response to the Notification letter (SE0012012) containing additional information on the new and predicate products, including information on design features[3], ingredients and materials. On January 27, 2016, FDA received a request to delay review of Smokin Joes' SE Reports (SE0012816). On March 11, 2016, FDA issued a General Correspondence letter stating that there is no timeframe for response currently requested in an A/I Request or Preliminary Finding letter (PFind), so there is no basis for an extension request. FDA had conversations with the applicant regarding all products currently submitted under an application (e.g., SE Report) and on November 23, 2016, a General Correspondence letter was issued where FDA agreed to delay review until March 10, 2017 as long as certain conditions were met by Smokin Joes. This delay in review enabled Smokin Joes to provide information, similar to the information requested in the August 19, 2016 PFind letter and the September 7, 2016 A/I Request letter issued to SE Reports in other Smokin Joes batches[4], for these SE Reports. On March 10, 2017, FDA received a partial response to the November 23, 2016 General Correspondence letter (SE0013970)[3], as well as certificates of analysis (SE0013969)[3]. On March 24, 2017, FDA received an unsolicited amendment requesting an extension of time to provide the remainder of their response to the November 23, 2016 General Correspondence letter due to the inability of Smokin Joes' contract testing laboratory to provide the product testing data needed to respond to FDA's requests (SE0013992). On June 16, 2017, a General Correspondence letter was issued granting the applicant until July 10, 2017 to respond to the November 23, 2016 General Correspondence letter.

On July 10, 2017, FDA received the response to the June 16, 2017 General Correspondence letter (SE0014198)[3]. On September 13, 2017, FDA issued an A/I Request letter with a response due date of November 12, 2017. On October 19, 2017, FDA received an amendment requesting an extension of time to respond to the A/I Request letter (SE0014381). On November 8, 2017, FDA denied this extension request. No response was received from the applicant by the

[2] A Notification letter issued later with instructions regarding amendments and the start of the substantive scientific review process.
[3] The design information in this amendment conflicted with the initial SE Report, without a clarification of which was in error.
[4] The August 19, 2016 PFind letter was issued to SE0004614-SE0004642 and SE0004978 – SE0004990. The September 7, 2016 A/I Request letter was issued to SE0005322, SE0005357-SE0005358, SE0005369-SE0005370, and SE0005422-SE0005424.

A/I Request letter response due date of November 12, 2017. On February 9, 2018, a PFind letter conveying all deficiencies and requests previously stated in the September 13, 2017 A/I Request letter was issued, with a response due date of March 11, 2018. To date, no response to the February 9, 2018 PFind letter has been received. On February 15, 2018, FDA provided a courtesy call to Smokin Joes to verify they received the PFind letter and understood the response was due March 11, 2018. Smokin Joes verified receipt of the letter but stated they would not be able to respond to this letter or any other deficiency letters for other STNs 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 Natural Silver 100 Size Box Fire Safe	SE0003026	SE0004569 SE0006310 SE0007587 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Natural Silver 100 Size Soft Pack Fire Safe	SE0003027	SE0004569 SE0006310 SE0007588 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

Product Name	SE Report	Amendments
Smokin Joes Natural Silver King Size Box Fire Safe	SE0003028	SE0004569 SE0006310 SE0007589 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Natural Silver King Size Soft Pack Fire Safe	SE0003029	SE0004569 SE0006310 SE0007590 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Natural White 100 Size Box Fire Safe	SE0003030	SE0004569 SE0006310 SE0007591 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381

Product Name	SE Report	Amendments
Smokin Joes Natural White 100 Size Soft Pack Fire Safe	SE0003031	SE0004569 SE0006310 SE0007592 SE0009117 SE0009439 SE0012012 SE0012816 SE0013969 SE0013970 SE0013992 SE0014198 SE0014381
Smokin Joes Natural White King Size Soft Pack Fire Safe	SE0003032	SE0004569 SE0006310 SE0007593 SE0009117 SE0009439 SE0012012 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 for SE0003026-SE0003031
- December 28, 2012 and May 9, 2013 for SE0003032

These reviews conclude that the SE Reports are administratively incomplete because the heating source of the new and predicate tobacco products was not included in the SE Reports. However, this information was provided by the applicant in amendment SE0012012. Therefore, these 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 July 29, 2015 conclude that the evidence submitted by the applicant is adequate to demonstrate that the predicate tobacco products are grandfathered and, therefore, are eligible predicate tobacco products.[5]

Because the new tobacco products are not substantially equivalent to the predicate tobacco products, OCE did not complete reviews to determine whether the new tobacco products are in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C) (See 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

Chemistry reviews[6] were completed by Tianrong Cheng on March 18, 2016 and Margaret Schmierer on August 31, 2017.

The final chemistry review concludes that the new tobacco products have different characteristics related to product chemistry compared to the corresponding predicate tobacco products and that the SE Reports do not contain sufficient detail to determine that the differences with respect to product composition 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 provide a detailed list of ingredients for all new and corresponding predicate tobacco products. However, all of your SE Reports also contain several discrepancies. For example:

    a. Ingredient quantities given in the SE Reports do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Reports.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for each predicate tobacco product does not match with the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

[5] Addendum reviews were completed on April 25, 2018 to include characterizing flavor for the predicate products; the conclusions in these addendum reviews did not differ from that in the original July 29, 2015 reviews.
[6] The review by Margaret Schmierer replaces/supersedes the review by Tianrong Cheng.

FDA needs clarification on these points to evaluate all new and predicate tobacco products and determine if the new tobacco products raise different questions of public health. Provide clarification on whether you expect information in amendments to replace or complement previous submissions. Additionally, provide clarification on all ingredient quantities by explaining the meaning of shaded cells and the reason for the discrepancy with total tobacco quantity in all predicate tobacco products. Further, provide all ingredient quantities as individual values, with associated variability. All quantities, given either as a measured value with measurement variability or as a target value with upper and lower range limits, should be in mg/cigarette. If any of this information cannot be provided, provide scientific evidence and rationale for why the lack of information should not raise different questions of public health in any of the new tobacco products.

2. All of your SE Reports provide HPHC data for the new and "present day predicates" (remanufactured predicates), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco products, is because the grandfathered products are not currently available, and state the remanufactured predicate tobacco products are made with the same materials and components as the grandfathered products, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco products are consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. Therefore, to evaluate the validity of the HPHC data, provide a clear statement or sufficient documentation showing your remanufactured predicate tobacco products are consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered products, and thus, the HPHC yields from the remanufactured predicate tobacco products are reflective of the HPHC yields from the corresponding grandfathered product. Also, provide a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested.

3. All of your SE Reports provide HPHC data for the new and remanufactured predicate tobacco products, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco products in SE0003028 - SE0003032 have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco products. In SE0003028, SE0003029, and SE0003032, the nicotine yields are 11–21% higher for the new tobacco products under the ISO smoking regimen. In SE0003028–SE0003032, the nicotine yields are 10–56% higher for the new tobacco products under the CI smoking regimen. You have not provided any scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needs this information. Provide scientific evidence and

rationale for why the higher nicotine yields in SE0003028–SE0003032 do not raise different questions of public health.

4. All of your SE Reports provide HPHC data for new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco products compared to the corresponding predicate tobacco products. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco products. Higher quantities of combusted sugars raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) [redacted] raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and corresponding predicate tobacco products may cause the new tobacco products to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needs you to provide scientific evidence and rationale to address why any differences do not cause the new tobacco products to raise different questions of public health. One way to provide such data is to measure mainstream smoke yields for the following two HPHCs:

    a. Acrolein
    b. Formaldehyde

    If the mainstream smoke yields of acrolein or formaldehyde are higher for the new tobacco products, relative to the corresponding predicate tobacco products, provide adequate scientific evidence and rationale as to why the higher HPHC yields do not cause the new tobacco products to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would best characterize the delivery of constituents from these products. FDA suggests that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures include, but are not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within similar timeframe. Provide the following information about HPHC testing so that we can fully evaluate the differences in HPHC quantities between the new and predicate new tobacco products:

    c. Reference product datasets (e.g., 1R6F)
    d. Quantitative test protocols and method used
    e. Validation reports for methods used
    f. Testing laboratory and their accreditation(s)
    g. Length of time between date(s) of manufacture and date(s) of testing
    h. Number of replicates
    i. Standard deviation(s)
    j. Complete data sets
    k. A summary of the results for all testing performed
    l. Storage conditions prior to initiating testing

If your test methods are national or international test standards, identify any deviations from those standards.

If the predicate tobacco product is not available for testing, you may choose to pursue other options to demonstrate substantial equivalence. Below are some options, though other alternative options may be acceptable. For example, you can manufacture the predicate tobacco product at present day, consistent with the product composition and design specifications in place at the time the grandfathered predicate tobacco product was originally manufactured. In this case, the mainstream smoke HPHC data should be accompanied by documentation to demonstrate the manufacture of the predicate tobacco product at present day, is reflective of the grandfathered predicate tobacco product at the time of original manufacture. Another option is to submit mainstream smoke HPHC data for products other than the predicate and new tobacco products (referred to as surrogate tobacco products) that can be extrapolated to the new and predicate tobacco products. In this case, data for the surrogate tobacco products may be submitted in place of data for the new and predicate tobacco products. However, the data should demonstrate 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. To extrapolate such data, the surrogate tobacco products should be as similar as possible in characteristics to the new and predicate tobacco products, and you should provide enough information to demonstrate these comparisons are valid. In addition to the smoke data, you should also submit information comparing the surrogate tobacco products to the new and predicate tobacco products.

All of the deficiencies included above refer to the lack of meaningful detail in all of the SE Reports and seek additional information to allow the reviewer to make an accurate evaluation of the new and predicate tobacco products. Although much of the detail of the ingredients are missing in all of the SE Reports, the applicant has claimed that (b) (4) [redacted], [redacted] are added to the new tobacco products, when none was included in the predicate tobacco products. Sugars and humectants like those added to the new tobacco products may result in increases in carbonyls including formaldehyde and acetaldehyde. These additives may also result in changes in the user behaviors. The applicant provided no information to address potential increases in HPHCs or the potential changes in user behaviors. The changes to the tobacco blend and ingredients may lead to changes in the amount of TNCO, acetaldehyde, benzene, and B[a]P, in the smoke under both ISO and CI smoking regimens. The applicant provided smoke data, but the applicant's data was obtained using a remanufactured predicate tobacco product that was not adequately described. Information about the remanufactured predicate, including details on tobacco blend, and design features, is needed before FDA can extrapolate test data from a remanufactured predicate to either the new or predicate tobacco product. Without knowing these details of the remanufactured predicate product, FDA was unable to evaluate the HPHC data collected using the remanufactured predicate. As indicated above, the remanufactured predicate tobacco products contain insufficient information to demonstrate that they are the same as the predicate tobacco products. However, if the applicant had provided this information, there are still concerns about the information that was provided and the analytes tested. The provided analytical data in SE0003028–SE0003032 indicate increases in nicotine content in the new tobacco products when compared to the invalid remanufactured predicate tobacco products.

FDA needed a rationale as to why this increase does not cause the new tobacco products to raise different questions of public health.

Therefore, the review concludes that there was inadequate information from a chemistry perspective to determine 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.

4.2. ENGINEERING

Engineering reviews[7] were completed by Beth A. Tirio on March 21, 2016 and Aarthi Arab on August 30, 2017.

The final engineering review concludes that the new tobacco products have different characteristics related to product engineering compared to the corresponding predicate tobacco products and that the SE Reports do not contain sufficient detail to determine that the differences with respect to product engineering 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 provide information on the design parameters for the new and predicate tobacco products but it is not clear that the information has been provided for the SE Reports in this batch. Your SE Reports do not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, it is necessary to compare key design parameters. Provide the **upper and lower range limits** for *all* the following cigarette design parameters for each new and predicate tobacco product:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)
    c. Filter denier per filament (dpf)

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

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)
    f. Tobacco filler mass (mg)

    For each new tobacco product, you state that the data provided for the tobacco filler mass and tobacco rod density is "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflects a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products is listed as an approximation. An exact target specification is needed to characterize filler mass. Provide the **target**

[7] The review by Aarthi Arab replaces/supersedes the review by Beth Tirio.

specification and upper and lower range limits for *all* the following cigarette design parameters for each new tobacco product:

g. Tobacco filler mass (mg)
h. Tobacco rod density (g/cm^3)

For each predicate tobacco product, the target specification data provided for the tobacco filler mass is listed as an approximation. The exact target specification is needed to characterize the design parameter. Provide the **target specification** for the following cigarette design parameter for each predicate tobacco product:

i. Tobacco filler mass (mg)

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., filter denier per filament and filter total denier if you choose to submit filter efficiency instead), state as such and provide a scientific rationale. If a difference exists between the new and corresponding predicate tobacco 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 tobacco product to raise different questions of public health.

Note that filter density, denier per filament, and total denier are necessary because filter efficiency (%) was not provided. As an alternate to submitting the information described above for filter density, 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 include design parameter specifications but do not include data confirming that specifications are met and it is not clear that the data provided is for the SE Reports in this batch. 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* the following cigarette design parameters for each new and predicate tobacco product:

   a. Overall cigarette draw resistance (mm H_2O)
   b. Tobacco filler mass (mg)
   c. Tobacco moisture (%)
   d. Filter ventilation (%)
   e. Filter density (g/cm^3)

   You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacks complete information to indicate that the target specifications have been met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products in SE0003026, SE0003027, SE0003030, and SE0003031 does not appear to be for the tow used in those products. 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* the following cigarette design parameters for each predicate and new tobacco product, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) – new tobacco products only
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

For each of the above parameters, provide the necessary data on a per unit of product basis (e.g., tobacco filler mass should be reported in mg 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 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, and it should be clear which COA should be used for which product.

Additionally, for the design parameters listed above that were tested per 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. All of your SE Reports require clarification regarding the materials used in the new and predicate tobacco products. All of your SE Reports *except* SE0003028 indicate that the new tobacco products may have multiple cigarette paper base paper materials because, as you state, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." 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). Each identified new and predicate tobacco product must consist of a single combination of cigarette paper base paper materials. Identify the following:

   a. Every unique material combination in the predicate tobacco product that you are comparing to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
   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.

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

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

c. Base paper basis weight (g/m^2)
d. Base paper porosity (CU)
e. Band porosity (CU)
f. Band width (mm)
g. Band space (mm)
h. Cigarette draw resistance (mmH_2O)

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* the following design parameters for each material in each new and predicate tobacco product:

i. Base paper basis weight (g/m^2)
j. Base paper porosity (CU)
k. Band porosity (CU)
l. Band width (mm)
m. Band space (mm)
n. Cigarette draw resistance (mmH_2O)

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

Option 1: Identify a single unique predicate tobacco product (with corresponding ingredients), composed of a single cigarette paper base paper material. Additionally, select and identify a single new tobacco product (with corresponding ingredients), composed of a single cigarette paper base paper material. The identified new tobacco product will be the only version of the new tobacco product considered for evaluation of substantial equivalence with the identified predicate

tobacco product. The identified new tobacco 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 base paper basis weight, base paper porosity, band porosity, band width, band space, overall cigarette draw resistance, and HPHCs for the unique new and predicate tobacco products, based on the single combination of cigarette paper base paper materials identified. If a difference exists between the single identified new tobacco product and the single identified predicate tobacco product, provide scientific evidence and a rationale for why the difference does not cause the new tobacco product to raise different questions of public health.

Option 2: If you need to list alternate materials for the new and predicate tobacco products, you may choose to demonstrate that the use of alternate cigarette paper base paper materials does not cause the new tobacco products to raise different questions of public health. To do this, identify every unique new and predicate tobacco product that may result from the integration of each combination of alternate materials. Each identified new and predicate tobacco 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 base paper basis weight, base paper porosity, band porosity, band width, band space, overall cigarette draw resistance, and HPHCs for each identified new and predicate tobacco product, based on all possible combinations of cigarette paper base paper materials. If a difference exists between the new and predicate tobacco products identified for each SE Report, provide scientific evidence and a rationale for why the difference does not cause the new tobacco product to raise different questions of public health.

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

- For one of the unique versions of the **new tobacco 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 tobacco 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 tobacco 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 **predicate tobacco 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 tobacco 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 base paper basis weight, base paper porosity, band porosity, band width, band space, overall cigarette draw resistance, and HPHCs for all the identified new and predicate tobacco products. If a difference exists between the identified new and predicate tobacco products, provide scientific evidence and a rationale for why the difference does not cause the new tobacco product to raise different questions of public health.

All predicate tobacco 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).

It is not clear whether the new and predicate tobacco products in SE0003028 have multiple cigarette paper base paper materials. Clarify whether a single cigarette paper base paper is used in each product in SE0003028. If multiple cigarette paper base paper is used in each product, provide the information described in the preceding paragraph for your other SE Reports.

4. All of your SE Reports contain inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. Therefore, confirm the target specifications and provide a rationale for the discrepancies for each of the following design parameters for the SE Reports and products listed:

    a. Filter length (mm): SE0003026, SE0003027, SE0003030, and SE0003031 – predicate tobacco products only
    b. Tobacco rod length: all SE Reports except SE0003028 – predicate tobacco products only
    c. Filter weight: all SE Reports except SE0003028 – new and predicate tobacco products
    d. Cigarette paper weight: all SE Reports except SE0003028 – new and predicate tobacco products
    e. Tipping paper weight: all SE Reports except SE0003028 – new and predicate tobacco products
    f. Cigarette paper seam adhesive weight: all SE Reports except SE0003028 – new and predicate tobacco products
    g. Tipping adhesive weight: all SE Reports except SE0003028 – new and predicate tobacco products

    Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, confirm the target specifications and upper and lower range limits and provide a rationale for the

discrepancies for each of the following design parameters for the SE Reports and products listed:

h. Cigarette length (mm): SE0003026, SE0003027, SE0003030, and SE0003031 – predicate tobacco products only
i. Cigarette diameter (mm): all SE Reports except SE0003028 – new tobacco products only
j. Cigarette paper base paper porosity (CU): all SE Reports except SE0003028 – new tobacco products only
k. Cigarette paper base paper porosity (CU): SE0003030 through SE0003032 – predicate tobacco products only

Additionally, in your June 24, 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 amendment, provide a rationale as to why the tipping paper is not long enough to completely cover the filter in SE0003026, SE0003027, SE0003030, and SE0003031. Furthermore, in the original submissions for all SE Reports *except* SE0003028, 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 in the amendment are in fact the correct tipping paper lengths. If you intended to report the tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission for SE0003026, SE0003027, SE0003030, and SE0003031. Therefore, confirm the target specifications and upper and lower range limits and provide a rationale for the discrepancies for the tipping paper length of the new and predicate tobacco products in all SE Reports, *except* SE0003028.

5. All of your SE Reports provide information on the design parameters; however, some of the design parameters need additional clarification to fully characterize the new and predicate tobacco products.

   a. For each new and predicate tobacco product, the tobacco moisture upper and lower range limits are reported as "±1%". Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification. Therefore, clarify the information and provide the upper and lower range limits for the tobacco moisture (%) for each new and predicate tobacco product.
   b. All of your SE Reports contain incomplete band spacing and band width information for the new tobacco products. You provide a data label that 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 tobacco products.
   c. For all predicate tobacco products, the range limits for filter density are 0.25 g/cm^3 higher and lower than the target specification. The target specification

varies between 0.126 g/cm^3 and 0.14 g/cm^3, depending on the SE Report and product. In addition, your March 2017 Amendment states that Exhibit B-2 provides a Celanese Acetate tow COA but this exhibit lacks filter density information. Review the predicate tobacco 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 tobacco 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 tobacco product to raise different questions of public health.

d. All of your SE Reports provide the new tobacco product "Band Porosity (CU)/Band Diffusion (cm/s)" target specifications in your June 24, 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, all your SE Reports except SE0003028 provide the new tobacco 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 tobacco product cigarette paper base paper porosity target specifications and range limits for all SE Reports using the accepted porosity unit of measure (CU).

e. Based on the information in your June 24, 2015 amendment, in SE0003032 the overall predicate tobacco product length is less than the sum of the filter and the tobacco rod. Review the predicate tobacco product tobacco rod length in SE0003032 and provide an explanation for why the overall cigarette length is less than the sum of the filter rod length and tobacco rod length.

f. All of your SE Reports need clarification regarding the filter design parameters. You provide denier information for the new and predicate tobacco products (labeled as "Total Denier / Denier per Filament") indicating that the total denier is 3.3 or 5.0, depending on the SE Report and product, and the denier per filament is 30,000. Because total denier is the mass of 9000 m of tow, this value is typically in the thousands. This interpretation of the data is supported by the standard naming convention for tow. Confirm that the target specifications for the filter total denier and denier per filament for all new and predicate tobacco products. If the typical tow naming convention accurately provides the total denier and denier per filament, provide a scientific justification for the 34% decrease in denier per filament in SE0003028, SE0003029, and SE0003032.

6. All of your SE Reports except SE0003028 report the new and predicate tobacco 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 tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for all new and predicate tobacco products. It is unclear if "Tip Ventilation Rate" is intended to represent filter ventilation. Furthermore, all your SE Reports previously provided tip ventilation and overall cigarette draw resistance target specifications and range limits based on computer model data that you have now withdrawn. In order fully characterize the filter ventilation (%) and overall draw resistance (mm H2O) provide the target specifications and range limits for the new and predicate tobacco products in all SE Reports.

7. All of your SE Reports include information on the filter design parameters of the new and predicate tobacco products. However, some of your SE Reports indicate design parameter differences that need additional information. 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. SE0003028, SE0003029, and SE0003032 show a filter pressure drop decrease of 11% in the new tobacco products as compared to the corresponding predicate tobacco products. The data you provided shows that there are substantial differences in TNCO and HPHC levels between the new and predicate tobacco products. Provide a scientific rationale with evidence as to why these differences to not raise different questions of public health.
    b. SE0003028, SE0003029, and SE0003032 show that the filter length of the new tobacco products decreased by 20% as compared to the corresponding predicate tobacco products. The data you provided shows that there are differences in TNCOs and HPHC levels between the new and predicate tobacco products. Provide a scientific rationale with evidence as to why these differences to not raise different questions of public health.
    c. SE0003028 shows that the base paper porosity of the new tobacco product decreased by 8% as compared to the predicate tobacco product. Provide a scientific rationale with evidence as to why this difference does not raise different questions of public health.

8. SE0003028, SE0003029, and SE0003032 report filter density, filter length, and filter circumference values for each predicate tobacco product. If the approximate filter weights for SE0003028, SE0003029, and SE0003032 are applied to calculate filter density, the new tobacco product filter densities would decrease ~8% as compared to the corresponding predicate tobacco products. Review the filter design parameter information and explain how the predicate tobacco product filter density value was determined in SE0003028, SE0003029, and SE0003032. If a difference exists between the new and corresponding predicate tobacco products, provide a rationale for each difference in the filter density target specification with evidence and a scientific discussion for why the difference does not cause the new tobacco product to raise different questions of public health.

9. All of your SE Reports include partial filter pressure drop test data for the new tobacco products. However, the information you provide is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. Confirm the filter pressure drop data points and range limits for all new tobacco products, address how product is handled when data falls outside of the range limits, and describe how future product specifications will be prevented from falling outside of range limits.

10. SE0003028 and SE0003029 show a puff count increase of 33% and SE0003032 shows an increase of 28% from the predicate tobacco products to the corresponding new tobacco products. The data you provided shows that there are differences in TNCO and HPHC levels between the new and predicate tobacco products. Provide a scientific rationale with evidence as to why these differences do not raise different questions of public health.

All of the SE Reports lack important information necessary demonstrate the product design characteristics of the new and predicate tobacco products are similar. All of the SE Reports lack sufficient information about filter length, filter ventilation, moisture content, tobacco filler mass, draw resistance, tobacco rod density, cigarette diameter, and filter tow specifications, targets, and/or supporting data for the new, predicate, or both tobacco products. These cigarette design specifications and measurements are important for the comparison of the new and predicate tobacco products. Without this information, FDA has inadequate information about product design; as such, it is not possible for FDA to determine the new tobacco products do not raise different questions of public health. In addition to lacking information about the filter design and tobacco filler design parameters, all of the SE Reports lack supporting test data and method descriptions for the cigarette paper base paper basis weight, cigarette paper base paper porosity, and cigarette paper base paper band porosity. For all of the SE Reports, except SE0003028, the information provided in the SE Reports does not match the information provided in supplements. In addition, all of the SE Reports, except SE0003028 state that alternative components are used in the manufacture of the new and predicate tobacco products causing confusion as to which of the target, upper and lower limits, provided in the SE Report were reported for the cigarette paper base paper band spacing, draw resistance, cigarette paper base paper band width, cigarette paper base paper band porosity, cigarette paper base paper porosity, cigarette paper base paper basis weight, cigarette paper weight, tipping paper basis weight, tobacco rod seam adhesive weight, tobacco rod length, and tipping paper seam adhesive weight. Without information about the materials and design parameters used in each of the products, it is not possible for FDA to determine if differences in these design parameters cause the new tobacco product to raise different questions of public health.

Despite the paucity of information outlined above, the applicant did provide some of the information needed to allow comparisons of the new and predicate tobacco products. In SE0003028, SE0003029, and SE0003032, the applicant states that there are filter pressure drop, calculated filter density, and filter length decreases in the new tobacco products as compared to the corresponding predicate tobacco products. Decreases in each of these parameters may lead to increases in the TNCO and HPHC smoke yield and a corresponding increase in user exposure to these smoke products. In addition, the puff count measured in the new tobacco products in SE0003028, SE0003029, and SE0003032 are reported to increase as compared to the corresponding predicate tobacco products. An increase in the puff count may lead to increases in the TNCO and HPHC smoke yield and a corresponding increase in user exposure to these smoke products. Finally, SE0003028 states that the cigarette paper base paper porosity of the new tobacco product decreased as compared to the predicate tobacco product. Decreases in cigarette paper base paper porosity may lead to increases in the TNCO and HPHC smoke yield and a corresponding increase in user exposure to these smoke products. The applicant did not provide a scientific rationale or evidence to demonstrate that the differences in the filter pressure drop, calculated filter density, filter length, puff count, and cigarette paper base paper porosity do not cause the new tobacco product to raise different questions of public health.

Therefore, the review concludes that there was inadequate information from an engineering perspective to determine 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.

4.3. TOXICOLOGY

Toxicology reviews were completed by Juan Crespo-Barreto on September 01, 2017 and Roxana Weil on July 25, 2016.

The final toxicology review concludes that the new tobacco products have different characteristics related to product toxicity compared to the corresponding predicate tobacco products and that the SE Reports do not contain sufficient detail to determine that the differences with respect to product toxicology 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 indicate apparent increases in the following HPHCs, relative to the corresponding remanufactured predicate tobacco products:

   - SE0003026 and SE0003027: acetaldehyde
   - SE0003028 and SE0003029: CO, acetaldehyde, B[a]P
   - SE0003030 and SE0003031: CO, acetaldehyde
   - SE0003032: CO, acetaldehyde, B[a]P

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

2. All of your SE Reports specify that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the corresponding predicate tobacco products. You indicate that the preservatives added to new tobacco products are a proprietary mixture, and limited information is provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and corresponding predicate tobacco products do not cause these new tobacco products to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco products are combustible cigarettes, the toxicological consequences of

exposure to the individual components (and their pyrolysis products) *via* the inhalation route needs to be addressed. Even if the individual ingredients are not available, provide scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco products to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route.

Because of the outstanding concerns of the chemistry and engineering reviewers about the validity of the data presented by the applicant, all deficiencies are discussed in as a comparison of apparent smoke yields of HPHCs. All of the SE Reports stated that the smoke of the new tobacco products contains higher levels of CO, acetaldehyde, or B[a]P than the corresponding predicate tobacco products. Because acetaldehyde and B[a]P are carcinogens, and carbon monoxide is a cardiovascular, reproductive, and developmental toxicant, increases in these smoke constituents may raise different questions of public health. In addition, the new tobacco products in all of the SE Reports include defoamers and preservatives in the seam adhesive that are not present in the predicate tobacco products. The applicant did not provide scientific evidence and rationale as to why the addition of these ingredients do not cause the new tobacco product 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 corresponding predicate tobacco products do not cause the new tobacco products to raise different questions of public health.

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:

- Higher quantity of flue-cured [redacted]
- Lower quantities of [redacted]
- Addition of expanded [redacted]
- Removal of [redacted]
- Addition of [redacted], [redacted], and [redacted]
- Higher quantity of [redacted] in rod paper (SE0003026–SE0003029 only)
- Higher quantity of defoamers and preservatives
- Higher quantity of [redacted] in seam adhesive
- Increase in acetaldehyde yield under CI regimen (SE0003026 and SE0003027 only)
- Increase in smoke yields of nicotine and acetaldehyde under ISO regimen and CO, TPM, nicotine, water, tar, and B[a]P under CI regimen (SE0003028 and SE0003029 only)
- Increase in CO, nicotine, and acetaldehyde under CI regimen (SE0003030 and SE0003031 only)
- Increase in smoke yields of CO and nicotine under ISO regimen and TPM, nicotine, water, tar, acetaldehyde, and B[a]P under CI regimen (SE0003032 only)

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. In all SE Reports, the applicant stated that there were increases in the [redacted], with corresponding decreases in [redacted] in the new tobacco products when compared to the corresponding predicate tobacco products. Increases in [redacted] may lead to increases in the B[a]P, while the decreases in the [redacted] each may lead to decreases in NNN and NNK. In addition to the changes in tobacco types in the new tobacco products, there was also an increase in expanded [redacted] and a reduction in [redacted]. These changes may lead to decreases in carbonyls but may lead to increases in TNCOs due to decreases tobacco rod density. All of the SE Reports also indicate increases in [redacted], [redacted], and [redacted] in the new tobacco products. In combination, increases in these ingredients may lead to increases in carbonyls, such as formaldehyde and acetaldehyde, and volatile organic compounds, like benzene. Changes in the product design may also effect the TNCO and other HPHCs. However, much of the information critical to understanding potential effects of the product design was not provided by the applicant, which limits FDA's ability to identify all of the potential HPHCs needed for comparison. The applicant provided data for all SE Reports that demonstrate increases in HPHC yields (specifically CO, acetaldehyde, and B[a]P) in the new tobacco products when compared to the corresponding remanufactured predicate tobacco products. However, the applicant did not provide sufficient information to demonstrate that the remanufactured predicate tobacco products are the same as the predicate tobacco products, thus this data is invalid for comparison of the new and predicate tobacco products. These deficiencies were communicated in letters to the applicant; however, they failed to respond to these letters. Therefore, there was inadequate information to determine that the new tobacco products do not raise different questions of public health.

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 determined that none exist. Therefore, the proposed action does not require preparation of an environmental assessment or an environmental impact statement.

NSE order letters should be issued for the new tobacco products in SE0003026, SE0003027, SE0003028, SE0003029, SE0003030, SE0003031, and SE0003032, as identified on the cover page of this review.

6.1. DEFICIENCIES FOR SE0003026

The NSE order letter for SE0003026 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[8]
    c. Filter denier per filament (dpf)[8]

    Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the predicate tobacco product:

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)
    f. Tobacco filler mass (mg)

    For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

[8] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided.

g. Tobacco filler mass (mg) [new and predicate]
h. Tobacco rod density (g/cm^3) [new tobacco product only]

Therefore, there was inadequate information to determine that the new tobacco products do not raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

   a. Overall cigarette draw resistance (mm H_2O)
   b. Tobacco filler mass (mg)
   c. Tobacco moisture (%)
   d. Filter ventilation (%)
   e. Filter density (g/cm^3)

   You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

   f. Cigarette paper base paper basis weight (g/m^2)
   g. Cigarette paper base paper porosity (CU)
   h. Cigarette paper band porosity (CU) [new tobacco product only]
   i. Filter denier per filament (dpf)
   j. Filter total denier (g/9000m)

   FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product."

However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
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 is considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for each of the following design parameters:

a. Filter length (mm) [predicate tobacco products only]
b. Tobacco rod length [predicate tobacco products only]
c. Filter weight [new and predicate tobacco products]
d. Cigarette paper weight [new and predicate tobacco products]
e. Tipping paper weight [new and predicate tobacco products]
f. Cigarette paper seam adhesive weight [new and predicate tobacco products]
g. Tipping adhesive weight [new and predicate tobacco products]

Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

h. Cigarette length (mm) [predicate tobacco products only]
i. Cigarette diameter (mm) [new tobacco products only]
j. Cigarette paper base paper porosity (CU) [new tobacco products only]

Additionally, in your June 24, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is different. If the tipping paper is 27 mm, as reported in the amendment, you should have provided a rationale as to why the tipping paper is not long enough to completely cover the filter. If you intended to report the

tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and a rationale for the discrepancies in the tipping paper length of the new and predicate tobacco product. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

    a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
    b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
    c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.
    d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.
    e. For the new and predicate tobacco products, denier information is labeled as "Total Denier / Denier per Filament," but the reported values did not match any of the standard naming convention for tow.

    Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H_2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a

determination that the new tobacco product does not raise different questions of public health.

7. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient

documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

10. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Report lacks additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) [redacted] may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

    a. Acrolein
    b. Formaldehyde

    If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA

needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

11. Your SE Report indicates an apparent increase in acetaldehyde relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHC is a carcinogen (acetaldehyde). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco product are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this

information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.2. DEFICIENCIES FOR SE0003027

The NSE order letter for SE0003027 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[9]
    c. Filter denier per filament (dpf)[9]

    Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the predicate tobacco product:

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)
    f. Tobacco filler mass (mg)

    For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

    g. Tobacco filler mass (mg) [new and predicate]
    h. Tobacco rod density (g/cm^3) [new tobacco product only]

    Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

    a. Overall cigarette draw resistance (mm H_2O)

[9] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided

b. Tobacco filler mass (mg)
c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
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 is considered a

single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for each of the following design parameters:

    a. Filter length (mm) [predicate tobacco products only]
    b. Tobacco rod length [predicate tobacco products only]
    c. Filter weight [new and predicate tobacco products]
    d. Cigarette paper weight [new and predicate tobacco products]
    e. Tipping paper weight [new and predicate tobacco products]
    f. Cigarette paper seam adhesive weight [new and predicate tobacco products]
    g. Tipping adhesive weight [new and predicate tobacco products]

    Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

    h. Cigarette length (mm) [predicate tobacco products only]
    i. Cigarette diameter (mm) [new tobacco products only]
    j. Cigarette paper base paper porosity (CU) [new tobacco products only]

    Additionally, in your June 24, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is different. If the tipping paper is 27 mm, as reported in the amendment, you should have provided a rationale as to why the tipping paper is not long enough to completely cover the filter. If you intended to report the tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and a rationale for the discrepancies in the tipping paper length of the new and predicate tobacco product. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.
d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.
e. For the new and predicate tobacco products, denier information is labeled as "Total Denier / Denier per Filament," but the reported values did not match any of the standard naming convention for tow.

Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

7. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits.

Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used,

validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

10. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4), (b)(4) are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

    a. Acrolein
    b. Formaldehyde

    If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

    c. Reference product datasets (e.g., 1R6F)
    d. Quantitative test protocols and method used
    e. Validation reports for methods used
    f. Testing laboratory and their accreditation(s)
    g. Length of time between date(s) of manufacture and date(s) of testing
    h. Number of replicates
    i. Standard deviation(s)
    j. Complete data sets
    k. A summary of the results for all testing performed
    l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

11. Your SE Report indicates an apparent increase in acetaldehyde relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHC is a carcinogen (acetaldehyde). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.3. DEFICIENCIES FOR SE0003028

The NSE order letter for SE0003028 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

a. Filter length (mm)
b. Filter total denier (g/9000 m)[10]
c. Filter denier per filament (dpf)[10]

Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the predicate tobacco product:

d. Cigarette diameter (mm)
e. Tobacco rod density (g/cm^3)
f. Tobacco filler mass (mg)

For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

g. Tobacco filler mass (mg) [new and predicate]
h. Tobacco rod density (g/cm^3) [new tobacco product only]

Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

a. Overall cigarette draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for

[10] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided

all the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

   a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
   b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
   c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.

   Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report includes information on the filter design parameters of the new and predicate tobacco products. However, your SE Report indicates design parameter differences that need additional information. You provided a limited explanation for these differences without a discussion on the impact to public health. FDA needed 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. You reported a filter pressure drop decrease of 11% in the new tobacco product as compared to the predicate tobacco product. The data you provided shows that there are substantial differences in TNCO and HPHC levels between the new and predicate tobacco products.
b. You reported that the filter length of the new tobacco product decreased by 20% as compared to the predicate tobacco product. The data you provided shows that there are differences in TNCOs and HPHC levels between the new and predicate tobacco products.
c. You reported that the base paper porosity of the new tobacco product decreased by 8% as compared to the predicate tobacco product.

Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

5. Your SE Report provided filter density, filter length, and filter circumference values for the predicate tobacco product. If the approximate filter weights are applied to calculate filter density, the new tobacco product filter density would decrease ~8% as compared to the predicate tobacco product. FDA needed an explanation of how the predicate tobacco product filter density value was determined. If a difference existed between the new and predicate tobacco product filter density values, FDA needed a rationale for each difference in the filter density target specification with evidence and a scientific discussion for why the difference did not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

6. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

7. Your SE Report demonstrates a puff count increase from the predicate tobacco product to the new tobacco product. The data you provided shows that there are differences in TNCO and HPHC levels between the new and predicate tobacco products. FDA needed a scientific rationale with evidence as to why these differences did not raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to

determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

10. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco product, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco product to have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco product. You have not provided scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needed this information. Without this evidence and rationale, FDA was unable to determine that the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

11. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) [redacted] may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

    a. Acrolein
    b. Formaldehyde

    If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report indicates an apparent increase in carbon monoxide, acetaldehyde, and benzo[a]pyrene relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHCs include carcinogens (acetaldehyde, B[a]P), cardiovascular, reproductive, and development toxicants (CO). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level in the new tobacco product does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

13. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and

predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.4. DEFICIENCIES FOR SE0003029

The NSE order letter for SE0003029 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[11]
    c. Filter denier per filament (dpf)[11]

    Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the predicate tobacco product:

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)
    f. Tobacco filler mass (mg)

    For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

    g. Tobacco filler mass (mg) [new and predicate]
    h. Tobacco rod density (g/cm^3) [new tobacco product only]

    Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

    a. Overall cigarette draw resistance (mm H_2O)
    b. Tobacco filler mass (mg)

[11] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided.

c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
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 is considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for the of the following design parameters:

    a. Tobacco rod length [predicate tobacco products only]
    b. Filter weight [new and predicate tobacco products]
    c. Cigarette paper weight [new and predicate tobacco products]
    d. Tipping paper weight [new and predicate tobacco products]
    e. Cigarette paper seam adhesive weight [new and predicate tobacco products]
    f. Tipping adhesive weight [new and predicate tobacco products]

    Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

    g. Cigarette diameter (mm) [new tobacco products only]
    h. Cigarette paper base paper porosity (CU) [new tobacco products only]

    Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

    a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
    b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
    c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.

d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.
e. For the new and predicate tobacco products, denier information is labeled as "Total Denier / Denier per Filament," but the reported values did not match any of the standard naming convention for tow.

Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

7. Your SE Report includes information on the filter design parameters of the new and predicate tobacco products. However, your SE Report indicates design parameter differences that need additional information. You provided a limited explanation for these differences without a discussion on the impact to public health. FDA needed 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. You reported a filter pressure drop decrease of 11% in the new tobacco product as compared to the predicate tobacco product. The data you provided shows that there are substantial differences in TNCO and HPHC levels between the new and predicate tobacco products.
    b. You reported that the filter length of the new tobacco product decreased by 20% as compared to the predicate tobacco product. The data you provided shows that there are differences in TNCOs and HPHC levels between the new and predicate tobacco products.

    Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provided filter density, filter length, and filter circumference values for the predicate tobacco product. If the approximate filter weights are applied to calculate filter density, the new tobacco product filter density would decrease ~8% as compared to the predicate tobacco product. FDA needed an explanation of how the predicate

tobacco product filter density value was determined. If a difference existed between the new and predicate tobacco product filter density values, FDA needed a rationale for each difference in the filter density target specification with evidence and a scientific discussion for why the difference did not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

9. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

10. Your SE Report demonstrates a puff count increase from the predicate tobacco product to the new tobacco product. The data you provided shows that there are differences in TNCO and HPHC levels between the new and predicate tobacco products. FDA needed a scientific rationale with evidence as to why these differences did not raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

11. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

13. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco product, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco product to have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco product. You have not provided scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needed this information. Without this evidence and rationale, FDA was unable to determine that the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

14. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients

in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) [redacted] may raise main stream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

a. Acrolein
b. Formaldehyde

If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

15. Your SE Report indicates an apparent increase in carbon monoxide, acetaldehyde, and benzo[a]pyrene relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in

tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHCs include carcinogens (acetaldehyde, B[a]P), cardiovascular, reproductive, and development toxicants (CO). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level in the new tobacco product does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

16. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.5. DEFICIENCIES FOR SE0003030

The NSE order letter for SE0003030 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[12]
    c. Filter denier per filament (dpf)[12]

[12] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided

Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new tobacco product:

d. Cigarette diameter (mm)
e. Tobacco rod density (g/cm^3)
f. Tobacco filler mass (mg)

For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

g. Tobacco filler mass (mg) [new and predicate]
h. Tobacco rod density (g/cm^3) [new tobacco product only]

Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

a. Overall cigarette draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]

i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

   a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
   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 is considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

   Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for each of the following design parameters:

   a. Filter length (mm) [predicate tobacco products only]
   b. Tobacco rod length [predicate tobacco products only]
   c. Filter weight [new and predicate tobacco products]
   d. Cigarette paper weight [new and predicate tobacco products]
   e. Tipping paper weight [new and predicate tobacco products]
   f. Cigarette paper seam adhesive weight [new and predicate tobacco products]
   g. Tipping adhesive weight [new and predicate tobacco products]

Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

h. Cigarette length (mm) [predicate tobacco products only]
i. Cigarette diameter (mm) [new tobacco products only]
j. Cigarette paper base paper porosity (CU) [new and predicate tobacco products]

Additionally, in your June 24, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is different. If the tipping paper is 27 mm, as reported in the amendment, you should have provided a rationale as to why the tipping paper is not long enough to completely cover the filter. If you intended to report the tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and a rationale for the discrepancies in the tipping paper length of the new and predicate tobacco product. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.
d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.

Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public Health.

7. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public

health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

10. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco product, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco product to have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco product. You have not provided scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needed this information. Without this evidence and rationale, FDA was unable to determine that the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

11. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream

smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b) (4) [redacted] may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

a. Acrolein
b. Formaldehyde

If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report indicates an apparent increase in carbon monoxide, acetaldehyde relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHCs

include carcinogen (acetaldehyde), cardiovascular, reproductive, and development toxicants (CO). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level in the new tobacco product does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

13. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.6. DEFICIENCIES FOR SE0003031

The NSE order letter for SE0003031 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[13]
    c. Filter denier per filament (dpf)[13]

    Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new tobacco product:

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)

[13] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided

f. Tobacco filler mass (mg)

For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco products was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

g. Tobacco filler mass (mg) [new and predicate]
h. Tobacco rod density (g/cm^3) [new tobacco product only]

Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

a. Overall cigarette draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product. However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

    a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
    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 is considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

    Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for each of the following design parameters:

    a. Filter length (mm) [predicate tobacco products only]
    b. Tobacco rod length [predicate tobacco products only]
    c. Filter weight [new and predicate tobacco products]
    d. Cigarette paper weight [new and predicate tobacco products]
    e. Tipping paper weight [new and predicate tobacco products]
    f. Cigarette paper seam adhesive weight [new and predicate tobacco products]
    g. Tipping adhesive weight [new and predicate tobacco products]

    Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed

confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

h. Cigarette length (mm) [predicate tobacco products only]
i. Cigarette diameter (mm) [new tobacco products only]
j. Cigarette paper base paper porosity (CU) [new tobacco products only]

Additionally, in your June 24, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is different. If the tipping paper is 27 mm, as reported in the amendment, you should have provided a rationale as to why the tipping paper is not long enough to completely cover the filter. If you intended to report the tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and a rationale for the discrepancies in the tipping paper length of the new and predicate tobacco product. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

   a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
   b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
   c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.
   d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.

Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public Health.

7. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters, indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

9. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

10. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco product, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco product to have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco product. You have not provided scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needed this information. Without this evidence and rationale, FDA was unable to determine that the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

11. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) (b)(4) are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different

questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

a. Acrolein
b. Formaldehyde

If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report indicates an apparent increase in carbon monoxide and acetaldehyde relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of this HPHC in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHCs include carcinogens (acetaldehyde), cardiovascular, reproductive, and development toxicants (CO). FDA needed sufficient evidence to demonstrate that the increased acetaldehyde level in the new tobacco product does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable

to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

13. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

6.7. DEFICIENCIES FOR SE0003032

The NSE order letter for SE0003032 should cite the following deficiencies:

1. Your SE Report does not include all the design parameters necessary to fully characterize the new and predicate tobacco products. To adequately characterize the products, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new and predicate tobacco products:

    a. Filter length (mm)
    b. Filter total denier (g/9000 m)[14]
    c. Filter denier per filament (dpf)[14]

    Additionally, FDA needed **upper and lower range limits** for *all* the following cigarette design parameters for the new tobacco product:

    d. Cigarette diameter (mm)
    e. Tobacco rod density (g/cm^3)
    f. Tobacco filler mass (mg)

    For the new tobacco product, you stated that the data provided for the tobacco filler mass and tobacco rod density was "based on data from scientific consultant's physical

[14] Note that denier per filament and total denier are needed because filter efficiency (%) was not provided

analysis of samples of the product." Thus, the data provided reflected a sample of the actual manufacturing outcome, not the target of the process, and cannot be used to characterize the design parameters. Furthermore, the target specification provided for the tobacco filler mass of the predicate tobacco product was listed as an approximation. FDA needed an exact **target specification and upper and lower range limits** for *all* the following cigarette design parameters:

g. Tobacco filler mass (mg) [new and predicate]
h. Tobacco rod density (g/cm^3) [new tobacco product only]

Without this information, FDA was unable to determine that any differences in the new tobacco product do not cause it to raise different questions of public health.

2. Your SE Report includes some of the design parameter specifications but does not include data confirming that specifications were met. FDA needed **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* the following cigarette design parameters for the new and predicate tobacco products:

a. Overall cigarette draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Tobacco moisture (%)
d. Filter ventilation (%)
e. Filter density (g/cm^3)

You also submitted documentation from the cigarette paper suppliers and filter tow suppliers as test data. However, the documentation lacked complete information to indicate that the target specifications were met for the cigarette paper base paper basis weight, cigarette paper base paper porosity, cigarette paper band porosity, filter total denier, or denier per filament. Furthermore, the documentation provided for the predicate tobacco products does not appear to be for the tow used in your product. FDA needed 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* the following cigarette design parameters for the predicate and new tobacco products, unless otherwise noted:

f. Cigarette paper base paper basis weight (g/m^2)
g. Cigarette paper base paper porosity (CU)
h. Cigarette paper band porosity (CU) [new tobacco product only]
i. Filter denier per filament (dpf)
j. Filter total denier (g/9000m)

FDA indicated that a certificate of analysis from the material supplier may have satisfied components of this deficiency. We stated that the COAs 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. The COA was to be a complete, unaltered COA from the material supplier, and it should have been clear which COA should be used for which product.

However, the COAs that were received did not provide this information. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

3. Your SE Report indicates that the new tobacco product may have multiple cigarette paper base paper materials because, as you stated, "it may be necessary to switch between the current [supplier's] product and the alternate [supplier's] product." However, 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. For FDA to determine if a listed material is an alternate material (due to differences in composition), we needed the following information for the new and predicate tobacco products, which consisted of a single combination of cigarette paper base paper materials:

    a. Every unique material combination in the predicate tobacco product that you compared to the new tobacco product in accordance with Section 910(a)(2)(B) of the FD&C Act.
    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 is considered a single new tobacco product and evaluated individually in accordance with Section 910(a)(2)(B) of the FD&C Act.

    Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

4. Your SE Report contains inconsistent information between the original submission and your June 24, 2015 amendment. You do not state if the information provided in the amendment supersedes the information provided in the original submission. FDA needed confirmation of the target specifications and rationale for the discrepancies for each of the following design parameters:

    a. Tobacco rod length [predicate tobacco products only]
    b. Filter weight [new and predicate tobacco products]
    c. Cigarette paper weight [new and predicate tobacco products]
    d. Tipping paper weight [new and predicate tobacco products]
    e. Cigarette paper seam adhesive weight [new and predicate tobacco products]
    f. Tipping adhesive weight [new and predicate tobacco products]

    Furthermore, the upper and lower range limit information you provided in your June 24, 2015 amendment was based on the corresponding target specification. Due to inconsistencies in the target specifications, it is not clear if the upper and lower range limits were intended to be used for any target specification value or only for the target specification provided in the June 24, 2015 amendment. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and rationale for the discrepancies for each of the following design parameters:

    g. Cigarette diameter (mm) [new tobacco products only]
    h. Cigarette paper base paper porosity (CU) [new and predicate tobacco products]

Additionally, in your June 24, 2015 amendment, tipping paper 'length' is identified as 27 mm while tipping paper 'width' is different. If the tipping paper is 27 mm, as reported in the amendment, you should have provided a rationale as to why the tipping paper is not long enough to completely cover the filter. If you intended to report the tipping paper 'width' as the 'length' in the June 24, 2015 amendment, there are discrepancies between the tipping paper length target values provided in the amendment and the original submission. Therefore, FDA needed confirmation of the target specifications and upper and lower range limits and a rationale for the discrepancies in the tipping paper length of the new and predicate tobacco product. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

5. Your SE Report provided information on the design parameters; however, some of the design parameters included information that need additional clarification for FDA to fully characterize the new and predicate tobacco products:

    a. For the new and predicate tobacco products, the tobacco moisture upper and lower range limits are reported as "±1%." Given that the target specification is also reported as a percent, it is unclear if the upper and lower range limits were taken to be ±1% of the target specification or if the applicant intended to report the range limits as 1% higher and lower than the target specification.
    b. For the new tobacco product, band spacing and band width information is incomplete. You provide a data label that 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.
    c. For the predicate tobacco product, the range limit for filter density are 0.25 g/cm^3 higher and lower than the target specification. However, this would lead to a negative lower range limit value, which is not achievable.
    d. For the new tobacco product, "Band Porosity (CU)/Band Diffusion (cm/s)" target specification is listed using "cm/s" as the unit of measure. Based on the data label, this implied that you reported the cigarette paper band diffusion. Diffusivity and porosity are not interchangeable. Furthermore, your SE Report provided the new tobacco product cigarette paper band porosity using "g" as the unit of measure. This is not an accepted porosity unit of measure. FDA needed to understand your intention for these values.
    e. For the new and predicate tobacco products, denier information is labeled as "Total Denier / Denier per Filament," but the reported values did not match any of the standard naming convention for tow.
    f. For the new and predicate tobacco products, you provide denier information (labeled as "Total Denier / Denier per Filament"), however the reported values did not follow any of the standard naming convention for tow.

    Without the necessary clarification to these points, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco product filter ventilation target specifications as <1%. This is not an exact value and prevents the complete characterization of the new and predicate tobacco products. Furthermore, in the June 24, 2015 amendment, you report the "Tip Ventilation Rate" for the new and predicate tobacco products. FDA was unclear if "Tip Ventilation Rate" was intended to represent filter ventilation. In order to fully characterize the filter ventilation (%) and overall draw resistance (mm H2O), FDA needed target specifications and range limits for the new and predicate tobacco products. Without this information, FDA cannot make a determination that the new tobacco product does not raise different questions of public health.

7. Your SE Report includes information on the filter design parameters of the new and predicate tobacco products. However, your SE Report indicates design parameter differences that need additional information. You provided a limited explanation for these differences without a discussion on the impact to public health. FDA needed 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. You reported a filter pressure drop decrease of 11% in the new tobacco product as compared to the predicate tobacco product. The data you provided shows that there are substantial differences in TNCO and HPHC levels between the new and predicate tobacco products.
    b. You reported that the filter length of the new tobacco product decreased by 20% as compared to the predicate tobacco product. The data you provided shows that there are differences in TNCOs and HPHC levels between the new and predicate tobacco products.

    Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

8. Your SE Report provided filter density, filter length, and filter circumference values for the predicate tobacco product. If the approximate filter weights are applied to calculate filter density, the new tobacco product filter density would decrease ~8% as compared to the predicate tobacco product. FDA needed an explanation of how the predicate tobacco product filter density value was determined. If a difference existed between the new and predicate tobacco product filter density values, FDA needed a rationale for each difference in the filter density target specification with evidence and a scientific discussion for why the difference did not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

9. Your SE Report included partial filter pressure drop test data for the new tobacco product. However, the information you provided is not complete and, therefore, cannot be used to confirm that the target specifications have been met. Because you did not provide quantitative acceptance criteria for the test data, the upper and lower range limits were used to determine if the test data met the specifications. Some of the test data points fell outside of the upper and lower range limits of these parameters,

indicating that the range limits may not be representative of the final product. FDA needed to understand the effects of data excursions upon the performance of the new tobacco product, how you address data that falls outside of the range limits, and how future product specifications will be prevented from falling outside of range limits. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

10. Your SE Report demonstrates a puff count increase from the predicate tobacco product to the new tobacco product. The data you provided shows that there are differences in TNCO and HPHC levels between the new and predicate tobacco products. FDA needed a scientific rationale with evidence as to why these differences did not raise different questions of public health. Without this information, FDA was unable to determine that any changes to the new tobacco product do not cause it to raise different questions of public health.

11. Your SE Report provides a detailed list of ingredients for the new and predicate tobacco products. However, your SE Report also contains several discrepancies. For example:

    a. Ingredient quantities given in the SE Report do not match ingredient quantities given in the June 2015 amendment, and it is unclear if the information in the amendment is supposed to replace or complement information presented in the original SE Report.
    b. All provided ingredient quantities are target quantities, often without upper or lower range limits.
    c. Some ingredient quantities are represented by shaded cells in the Excel spreadsheets, with no explanation of the intended meaning of a shaded cell.
    d. The provided total tobacco quantity for the predicate tobacco product does not match the calculated sum of the provided individual tobacco type quantities.
    e. Subcomponent ingredient quantities are in percentages, and in some cases percentage ranges, instead of individual target or measured values.
    f. Ingredient quantities in most adhesive components in the new and predicate tobacco products are in ranges, with no target quantity provided.

    FDA needed clarification on these points to evaluate the new and predicate tobacco products and determine if the new tobacco product raises different questions of public health. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

12. Your SE Report provides HPHC data for the new and "present day predicate" (remanufactured predicate), including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. You claim the use of the remanufactured predicate tobacco product is necessary because the grandfathered product is not currently available and state that the remanufactured predicate tobacco product is made with the same materials and components as the grandfathered product, as marketed on February 15, 2007. However, you did not provide sufficient documentation or clear explanations to support this claim. Without sufficient documentation or a clear explanation, FDA cannot sufficiently evaluate if the

remanufactured predicate tobacco product is consistent with the product design and composition of the original grandfathered product. Additionally, per your July 2017 amendment, different samples were stored at different temperatures for different lengths of time, with no rationale for why the different storage conditions would not affect results of HPHC testing. You also provided the names of the internal lab methods used, but with no additional description or explanation of the method procedures. To evaluate the validity of the HPHC data, FDA needed a clear statement or sufficient documentation showing that your remanufactured predicate tobacco product is consistent with the product design and composition (tobacco, ingredients other than tobacco, and materials) of the grandfathered product, and thus, the HPHC yields from the remanufactured predicate tobacco product are reflective of the HPHC yields from the grandfathered product. FDA also needed a detailed description of all methods used, validation reports for all methods used, and storage conditions, including temperature and length of time, for all samples tested. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

13. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco product, including measured values for nicotine, under both ISO and CI smoking regimens. However, the data provided shows the new tobacco product to have higher mainstream smoke yields of nicotine when compared to the remanufactured predicate tobacco product. You have not provided scientific evidence or rationale for why the higher nicotine yields do not raise different questions of public health. Nicotine is a known addictive chemical in tobacco products, so FDA needed this information. Without this evidence and rationale, FDA was unable to determine that the differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

14. Your SE Report provides HPHC data for the new and remanufactured predicate tobacco products, including measured values for TNCO, acetaldehyde, benzene, and B[a]P, under both ISO and CI smoking regimens. However, your Reports lack additional HPHC data FDA needs, because of significant differences in tobacco blend casing flavor ingredients in the new tobacco product compared to the predicate tobacco product. For example, (b)(4) [redacted], (b)(4) [redacted] are only present in the new tobacco product. Higher quantities of combusted sugars may raise the mainstream smoke yields of formaldehyde, acrolein, and benzene. Higher quantities of combusted humectants like (b)(4) [redacted] may raise mainstream smoke yields of acetaldehyde, acrolein, and formaldehyde. These differences between the new and predicate tobacco products may cause the new tobacco product to raise different questions of public health. To evaluate all ingredient differences between the new and predicate tobacco products, FDA needed scientific evidence and rationale to address why any differences did not cause the new tobacco products to raise different questions of public health. One way that such data could have been provided was to measure mainstream smoke yields for the following HPHCs:

    a. Acrolein
    b. Formaldehyde

If the mainstream smoke yields of acrolein or formaldehyde were higher for the new tobacco product, relative to the predicate tobacco product, FDA would need adequate scientific evidence and rationale as to why the higher HPHC yields did not cause the new tobacco product to raise different questions of public health. The measurement of HPHC quantities under both ISO and Canadian Intense smoking regimens would have best characterized the delivery of constituents from these products. FDA suggested that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures included, but were not limited to, using the same laboratory, the same type of smoking machine, the same methods, similar sample storage conditions and duration, and testing within a similar timeframe. In addition to the smoke data, FDA needed the following information about HPHC testing to fully evaluate the differences in HPHC quantities between the new and predicate tobacco products:

c. Reference product datasets (e.g., 1R6F)
d. Quantitative test protocols and method used
e. Validation reports for methods used
f. Testing laboratory and their accreditation(s)
g. Length of time between date(s) of manufacture and date(s) of testing
h. Number of replicates
i. Standard deviation(s)
j. Complete data sets
k. A summary of the results for all testing performed
l. Storage conditions prior to initiating testing

Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

15. Your SE Report indicates an apparent increase in carbon monoxide, acetaldehyde, and benzo[a]pyrene relative to the remanufactured predicate tobacco product. The increases in HPHC levels may reflect the overall consequences of the differences in characteristics between the new and predicate tobacco products, such as changes in tobacco blends, cigarette papers, adhesives, and flavor ingredients. Increases in smoke yields of these HPHCs in the new tobacco product as compared to their predicate tobacco product could result in increased HPHC exposures for users of the new tobacco product. The increased HPHCs include carcinogens (acetaldehyde, B[a]P), cardiovascular, reproductive, and development toxicants (CO). FDA needed sufficient evidence to demonstrate that the increased HPHC level in the new tobacco product does not cause the new tobacco product to raise different questions of public health. Without this information, FDA was unable to determine that differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.

16. Your SE Report specifies that the defoamers and preservatives added to the seam adhesive in the new tobacco products are different from the predicate tobacco product. You indicated that the preservatives added to the new tobacco product are a proprietary mixture, and limited information was provided regarding the identity and quantities of the subcomponents. The opinion by Perfetti and cited reference by

Coggins et al., (2013) are insufficient in providing product-specific supporting evidence to demonstrate that the differences in ingredients between the new and predicate tobacco products do not cause this new tobacco product to raise different questions of public health. To conduct a comprehensive toxicological evaluation, the detailed list of uniquely identifying information (e.g., grade/purity and ingredient quantities) of the compounds present in these complex ingredients is needed. Since the new tobacco product is a combustible cigarette, the toxicological consequences of exposure to the individual components (and their pyrolysis products) *via* the inhalation route needed to be addressed. Even if the individual ingredients are not available, FDA needed scientific evidence and rationale for why the addition of these ingredients does not cause the new tobacco product to raise different questions of public health when these ingredients and/or ingredient byproducts are taken in *via* the inhalation route. Without this information, FDA was unable to determine that any differences between the new and predicate tobacco products do not cause the new tobacco product to raise different questions of public health.